09/084,542

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L13              STRUCTURE UPLOADED
L14            0 S L13 SAM SUB=L***
L15          608 S L3 OR L12

     FILE 'CAPLUS' ENTERED AT 17:54:12 ON 17 MAY 2002
L16          141 S L15
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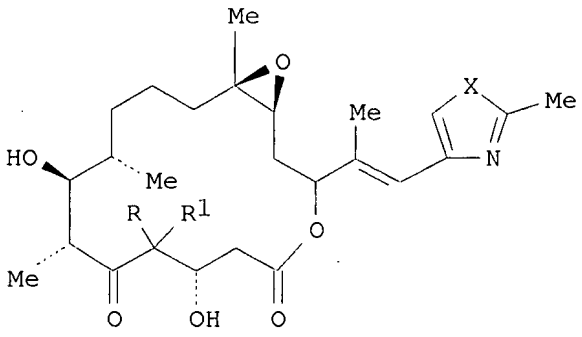
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	620.68	920.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-86.73	-86.73

STN INTERNATIONAL LOGOFF AT 17:59:03 ON 17 MAY 2002

L16 ANSWER 123 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1998:50907 CAPLUS
DN 128:180246
TI Total synthesis of oxazole- and cyclopropane-containing epothilone B analogs by the macrolactonization approach
AU Nicolaou, K. C.; Sarabia, Francisco; Finlay, M. Ray V.; Ninkovic, Sacha; King, N. Paul; Vourloumis, Dionisios; He, Yun
CS Department of Chemistry and The Skaggs Institute for Chemical Biology The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Chem.--Eur. J. (1997), 3(12), 1971-1986
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
GI



I

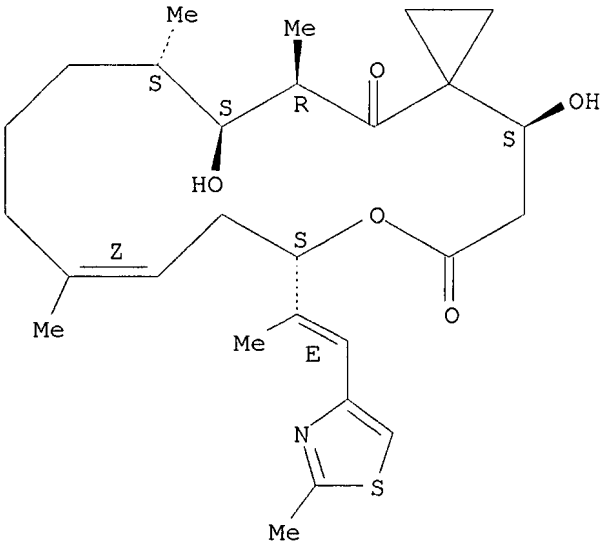
AB In order to probe structure-activity relationships in the epothilone area, two series of epothilone B analogs were designed and synthesized. The first series contg. an oxazole moiety in place of a thiazole on the side chain was constructed via utilization of key intermediates whereas the second series contg. an ethano group instead of the gem-di-Me group at position 4 was synthesized. A Yamaguchi-type macrolactonization reaction was used to construct the macrocycle from a secoacid, which was assembled, in both cases, via a) an aldol reaction, b) an Enders alkylation, and c) a Wittig-type reaction. This convergent strategy provided access to oxazole and 4,4-ethano analogs, e.g., I (R = R1 = Me, X = O, S; RR1 = CH2CH2, X = O, S).

IT **198571-48-1P 198571-60-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of oxazole- and cyclopropane-contg. epothilone B analogs via macrolactonization)

RN 198571-48-1 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-11,15,17-trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16S,17R)- (9CI) (CA INDEX NAME)

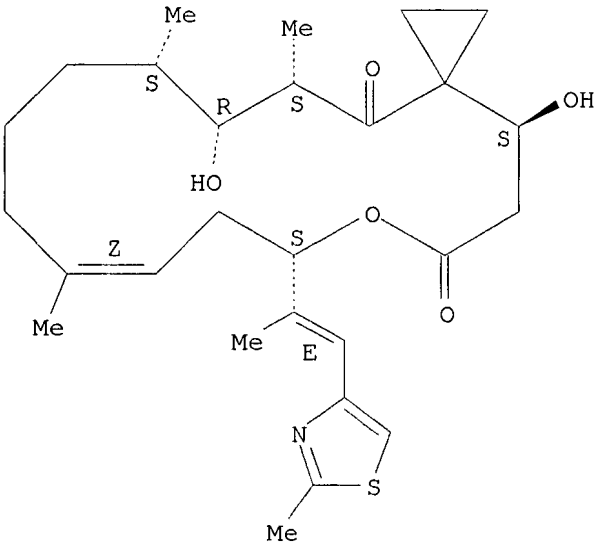
Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

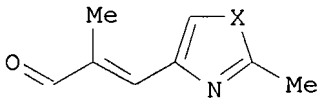


RN 198571-60-7 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-11,15,17-trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16R,17S)- (9CI) (CA INDEX NAME)

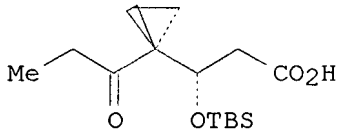
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L16 ANSWER 124 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1998:50906 CAPLUS
DN 128:140541
TI Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach
AU Nicolaou, K. C.; Vallberg, Hans; King, N. Paul; Roschangar, Frank; He, Yun; Vourloumis, Dionisios; Nicolaou, Christopher G.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Chem.--Eur. J. (1997), 3(12), 1957-1970
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
GI



I



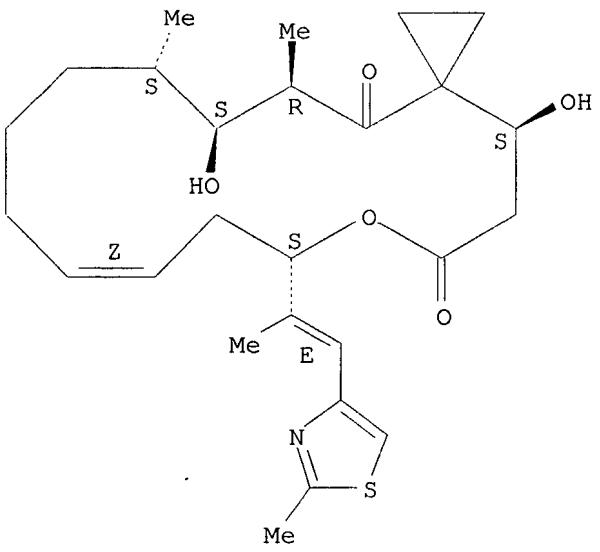
III

AB For structure-activity relationship studies, two series of epothilone A analogs have been designed and synthesized, one contg. an oxazole moiety instead of the thiazole heterocycle and the other contg. a spirocyclopropane moiety in place of the gem-di-Me group at position C-4 (4,4-ethano-epothilones). The olefin metathesis strategy in soln. was utilized for the chem. synthesis of these compds. starting with key building blocks (I) (X = O), (S)-H2C=CH(CH2)3CH(Me)CHO (II), (S)-MeCH2COCMe2CH(OSiMe2CMe3)CH2CO2H for the oxazole series and building blocks I (X = S), II, and (III) for the 4,4-ethano series. The convergent strategy towards the designed epothilone A series involved: a- an aldol condensation reaction, b- an esterification reaction, c- an olefin metathesis reaction catalyzed by [RuCl2(=CHPh)-(PCy3)2], and d- epoxidn. of the macrocycle double bond.

IT **198571-47-0P 198571-51-6P 198571-59-4P 198571-63-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of oxazole- and cyclopropane-contg. epothilone A analogs by the olefin metathesis approach)

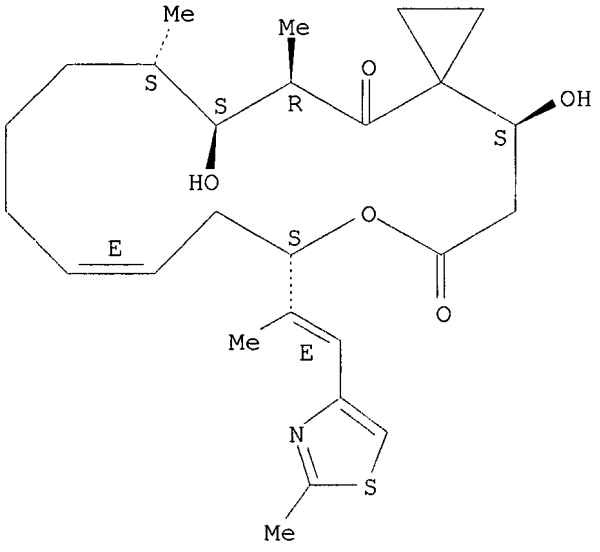
RN 198571-47-0 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,17-dimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16S,17R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-51-6 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10E,15S,16S,17R)-
(9CI) (CA INDEX NAME)

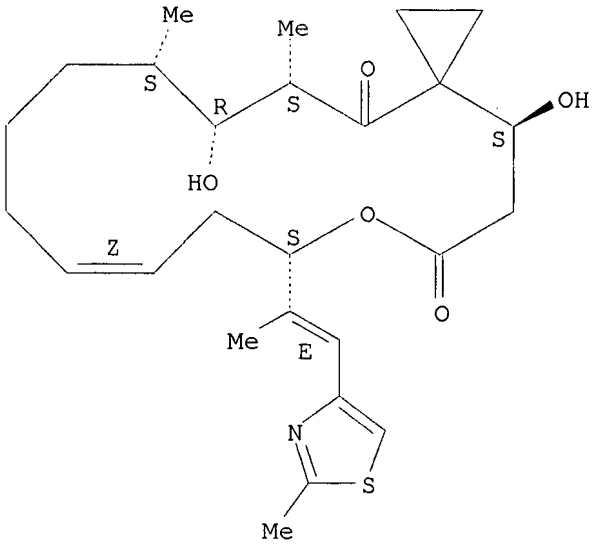
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 198571-59-4 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10Z,15S,16R,17S)-

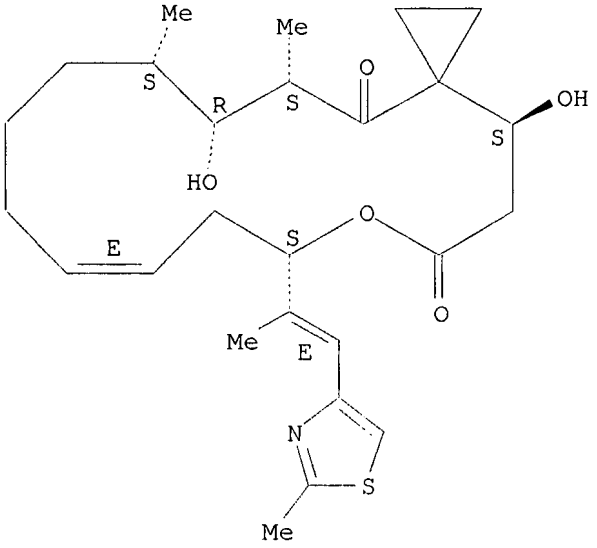
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



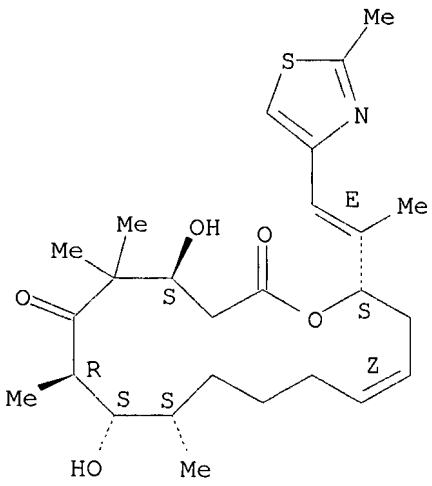
RN 198571-63-0 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10E,15S,16R,17S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



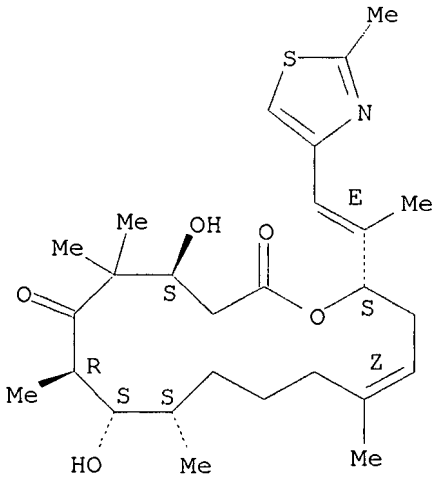
L16 ANSWER 125 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1998:729 CAPLUS
DN 128:88685
TI Metathesis vs metastasis: the chemistry and biology of the epothilones
AU Finlay, Ray
CS Dep. Chemistry, The Skaggs Inst. for Chemical Biol., The Scripps Res. Inst., La Jolls, CA, 92037, USA
SO Chem. Ind. (London) (1997), (24), 991-996
CODEN: CHINAG; ISSN: 0009-3068
PB Society of Chemical Industry
DT Journal; General Review
LA English
AB A review with 15 refs. on a recent entry onto the scene of potentially useful natural products, the epothilones A - E, providing valuable information for the fight against cancer via their interaction with microtubules.
IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(chem. and bioactivity of the epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.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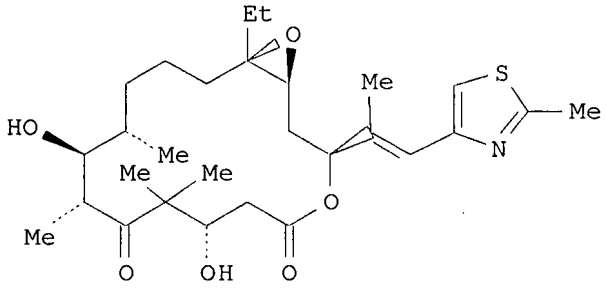
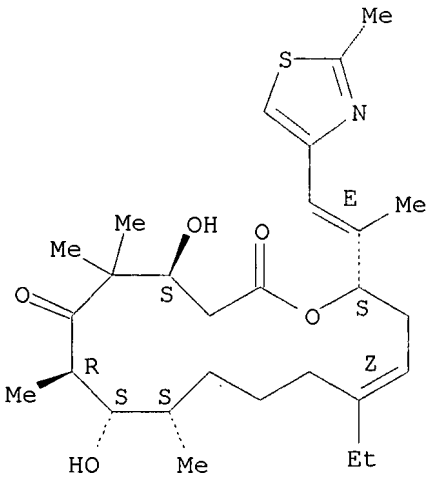
L16 ANSWER 126 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:787450 CAPLUS
DN 128:101936
TI Total synthesis of 26-hydroxyepothilone B and related analogs
AU Nicolaou, K. C.; Ninkovic, Sacha; Finlay, M. Ray V.; Sarabia, Francisco; Li, Tianhu
CS Department of Chemistry and Biochemistry, University of California, California, 92093, USA
SO Chem. Commun. (Cambridge) (1997), (24), 2343-2344
CODEN: CHCOFS; ISSN: 1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 128:101936
GI



I

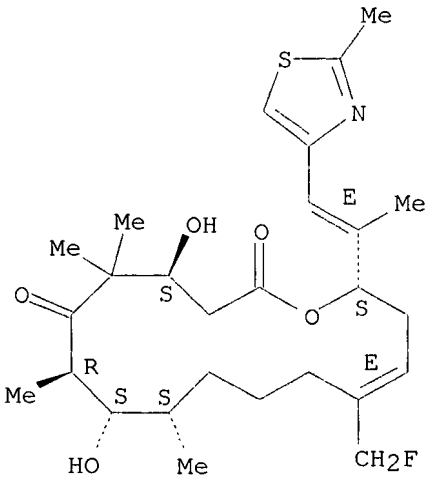
AB A series of 26-substituted epothilones B, e.g. I, were constructed by total synthesis involving a selective Wittig olefination, an aldol reaction and a macrolactonization as key steps.
IT **198475-04-6P 201136-91-6P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



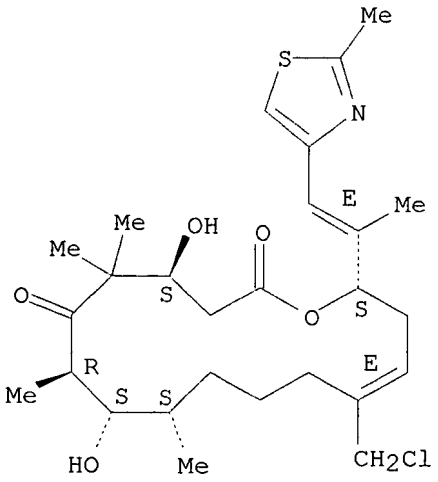
RN 201136-91-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-
tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



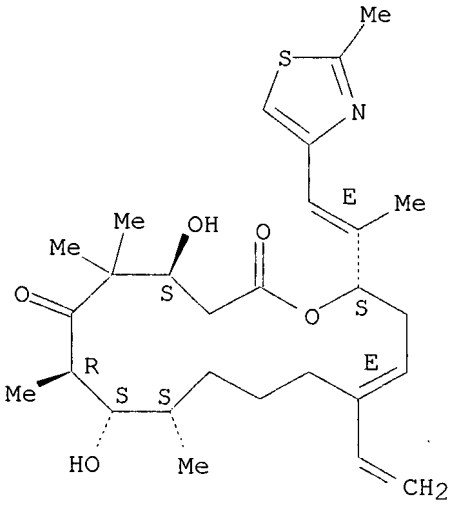
IT **201136-88-1P 201136-92-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 201136-88-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
13-(chloromethyl)-4,8-dihydroxy-5,5,7,9-
tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-92-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethenyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

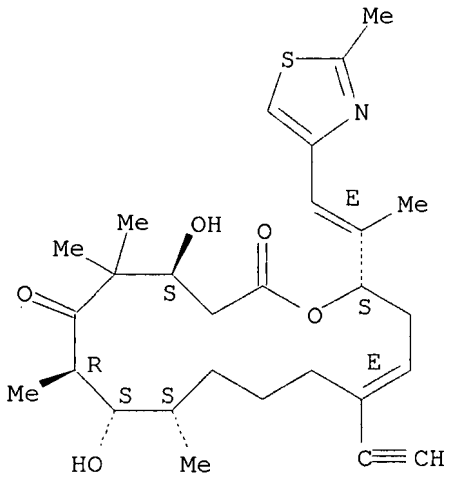
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **201136-94-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 201136-94-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethynyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,

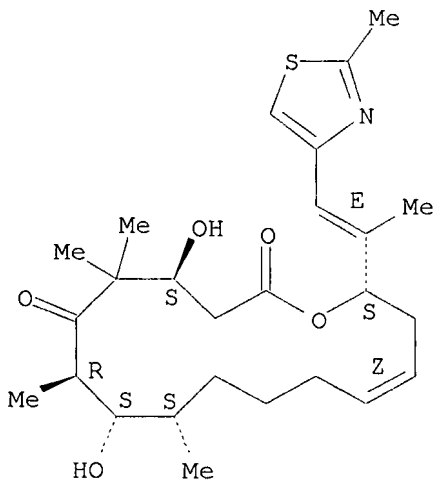
(4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L16 ANSWER 127 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:724919 CAPLUS
DN 127:346221
TI Synthesis of epothilones A and B in solid and solution phase. [Erratum to document cited in CA127:4950]
AU Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.
CS Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Nature (London) (1997), 390(6655), 100
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
AB Ref. 19, includes, in addn. to a total synthesis of epothilone B, biol. data for compd. 23 and other congeners similar to the reported in the Letter.
IT **186692-73-9P 189453-10-9P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a combinatorial library via solid-phase synthesis of epothilone A and soln.-phase synthesis of epothilone B (Erratum))
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

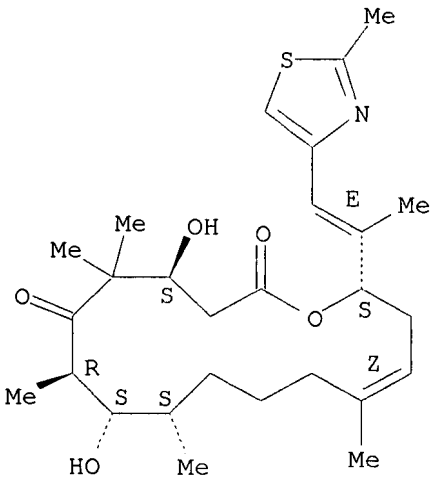
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

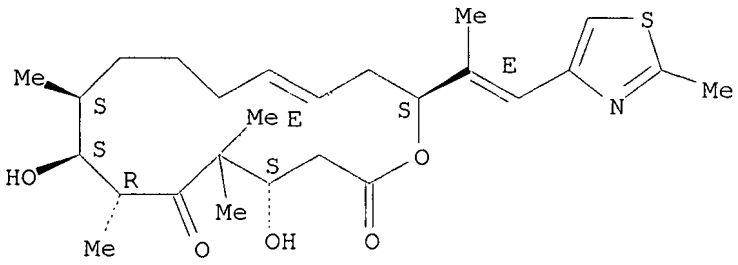
Double bond geometry as shown.



IT **188260-10-8P 189453-40-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a combinatorial library via solid-phase synthesis of epothilone A and soln.-phase synthesis of epothilone B (Erratum))

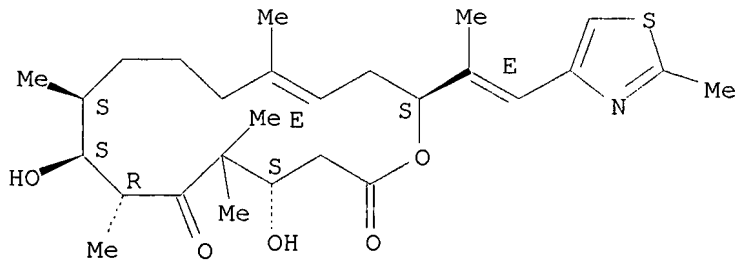
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.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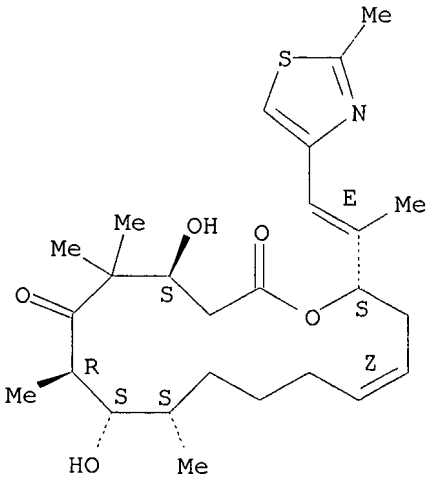
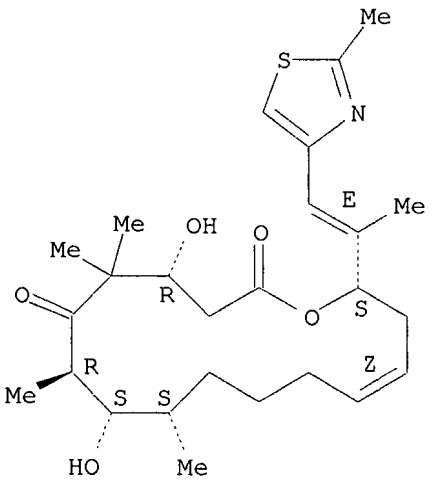
L16 ANSWER 128 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:714315 CAPLUS
DN 128:3560
TI Designed epothilones: combinatorial synthesis, tubulin assembly properties, and cytotoxic action against taxol-resistant tumor cells
AU Nicolaou, K. C.; Vourloumis, Dionisios; Li, Tianhu; Pastor, Joaquin; Winssinger, Nicolas; He, Yun; Ninkovic, Sacha; Sarabia, Francisco; Vallberg, Hans; Roschangar, Frank; King, N. Paul; Finlay, M. Ray V.; Giannakakou, Pareskevi; Verdier-Pinard, Pascal; Hamel, Ernest
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Angew. Chem., Int. Ed. Engl. (1997), 36(19), 2097-2103
CODEN: ACIEAY; ISSN: 0570-0833
PB Wiley-VCH
DT Journal
LA English
AB The title work demonstrates the power of interfacing combinatorial chem. with chem. biol. as facilitated by solid-phase synthesis, radiofrequency encoded combinatorial chem. and modern biol. assays. A library of 112 epothilones were prepd. by solid-phase synthesis, their structure activity relationships measured by tubulin binding assay and some tested for inhibition of carcinoma cell growth.
IT **186692-73-9P 188259-95-2P 188260-10-8P 188260-34-6P 189453-10-9P 189453-40-5P 193071-86-2P 193146-35-9P 198571-16-3P 198571-18-5P 198571-20-9P 198571-22-1P 198571-24-3P 198571-25-4P 198571-26-5P 198571-28-7P 198571-29-8P 198571-30-1P 198571-31-2P 198571-32-3P 198571-33-4P 198571-37-8P 198571-38-9P 198571-39-0P 198571-47-0P 198571-48-1P 198571-49-2P 198571-50-5P 198571-51-6P 198571-52-7P 198571-53-8P 198571-59-4P 198571-60-7P 198571-61-8P 198571-62-9P 198571-63-0P 198571-64-1P 198571-65-2P 198571-66-3P 198571-67-4P 198571-69-6P 198571-70-9P 198571-71-0P 198571-72-1P 198571-77-6P 198571-78-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combinatorial synthesis of epothilone library, tubulin assembly properties, and cytotoxic action against taxol-resistant tumor cells)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



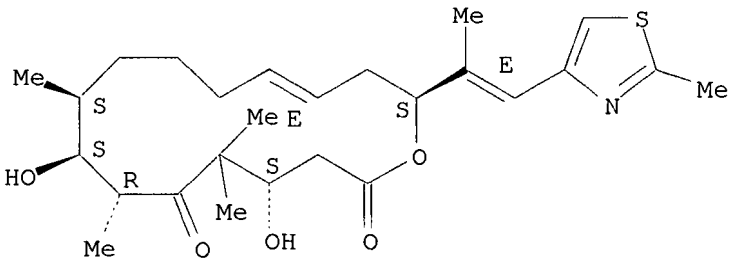
RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



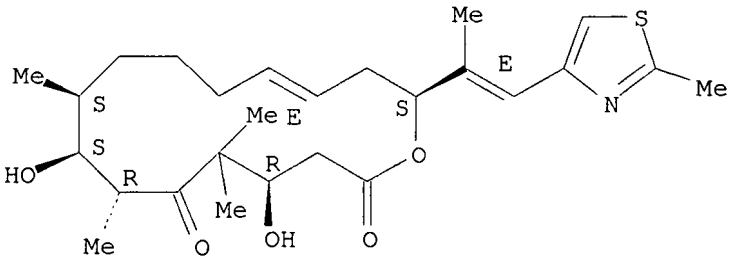
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



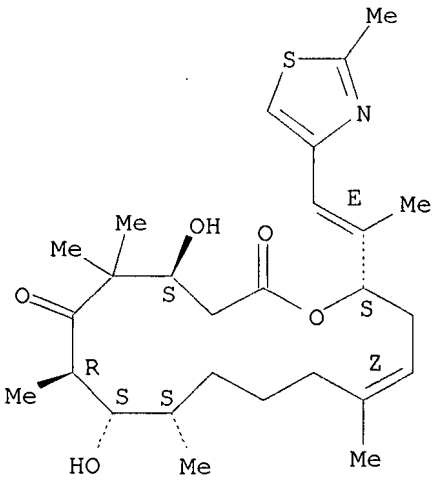
RN 188260-34-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



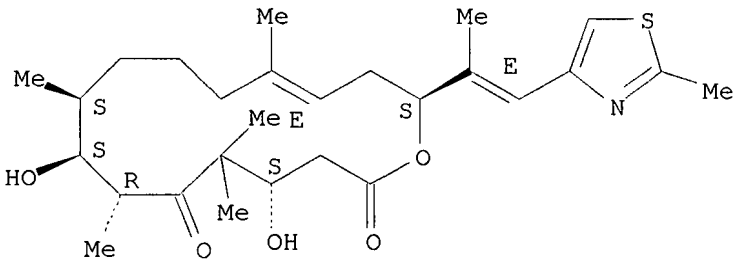
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



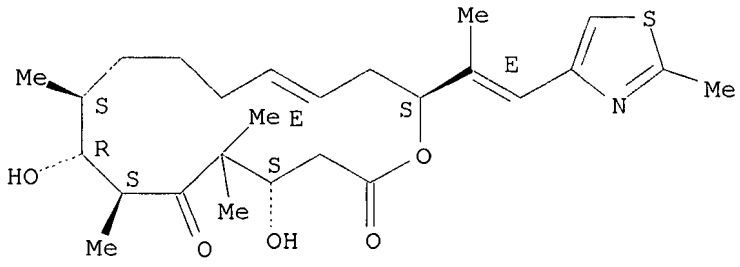
RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



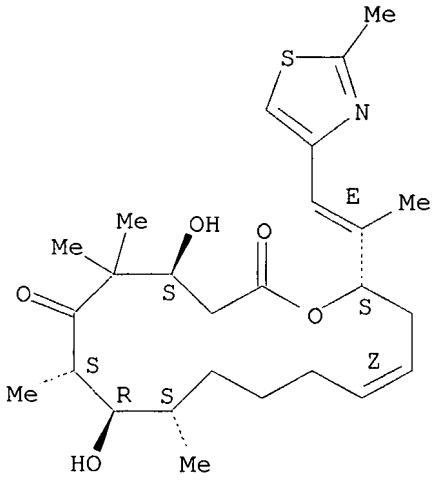
RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



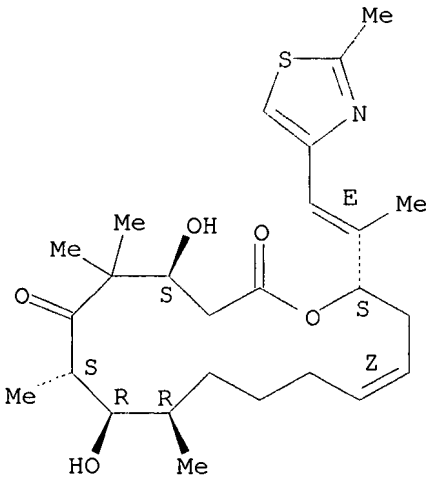
RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



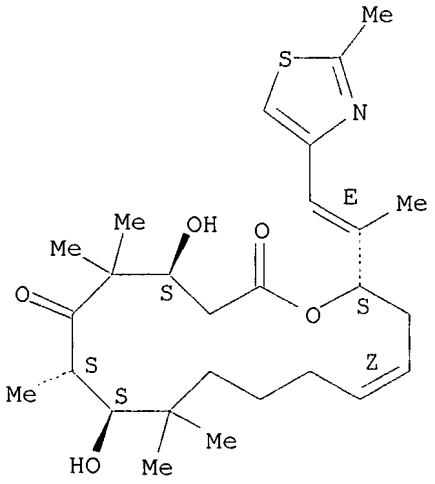
RN 198571-16-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



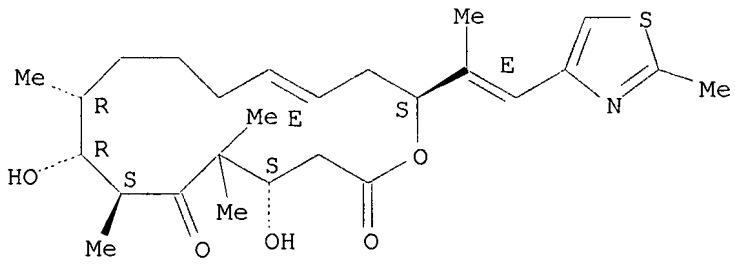
RN 198571-18-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



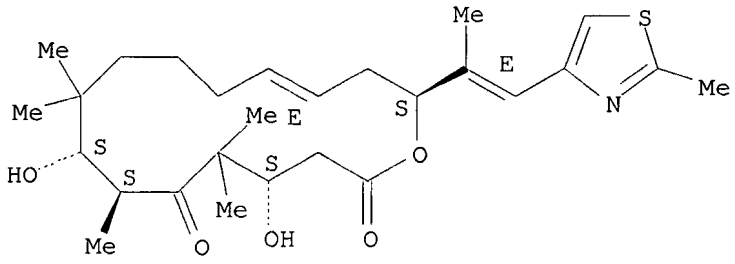
RN 198571-20-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



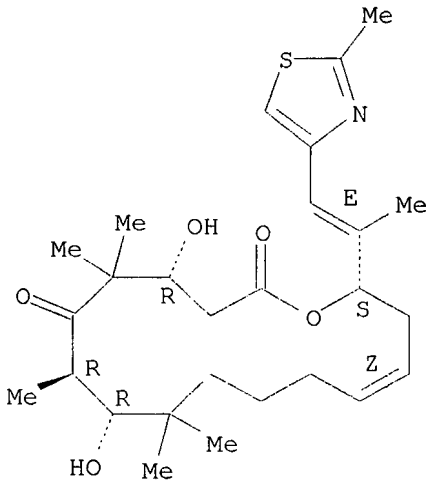
RN 198571-22-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



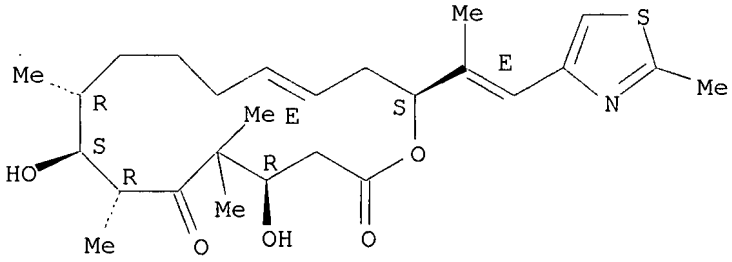
RN 198571-24-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



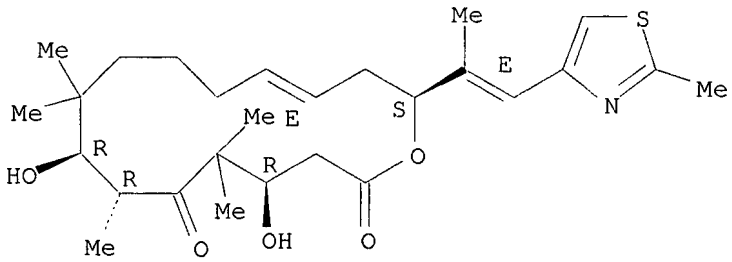
RN 198571-25-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



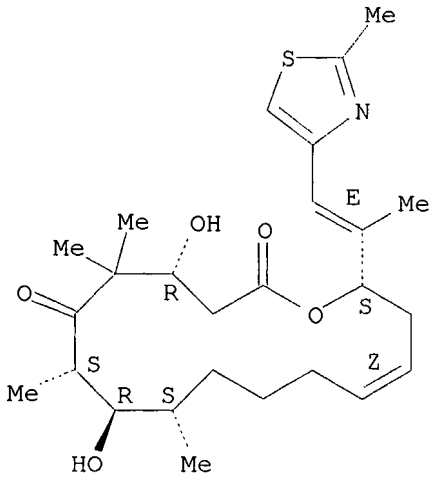
RN 198571-26-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



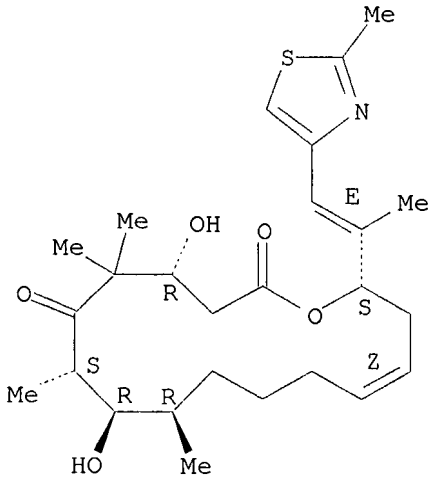
RN 198571-28-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



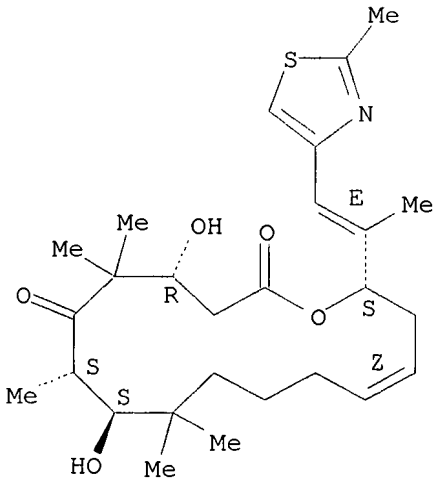
RN 198571-29-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



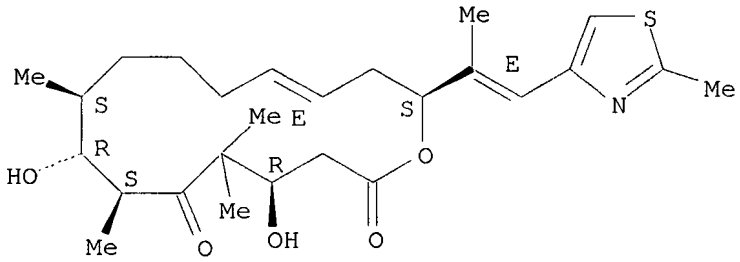
RN 198571-30-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



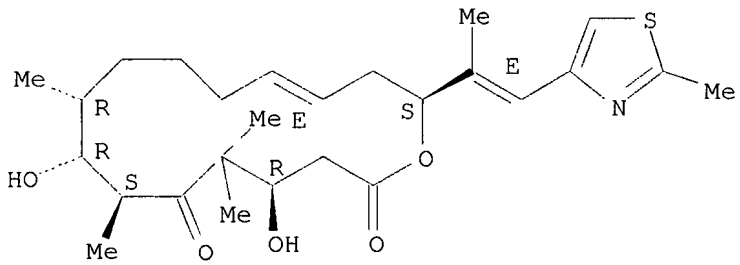
RN 198571-31-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



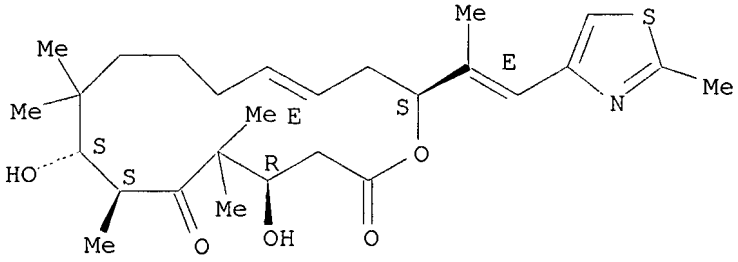
RN 198571-32-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



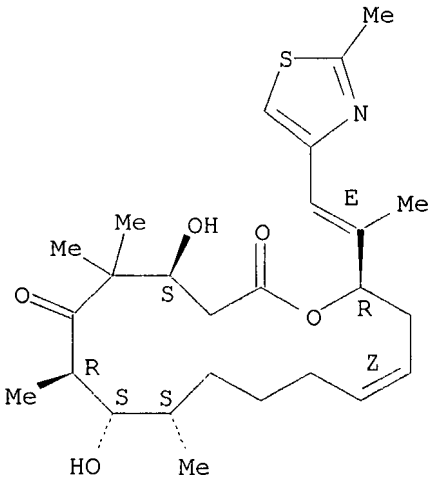
RN 198571-33-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



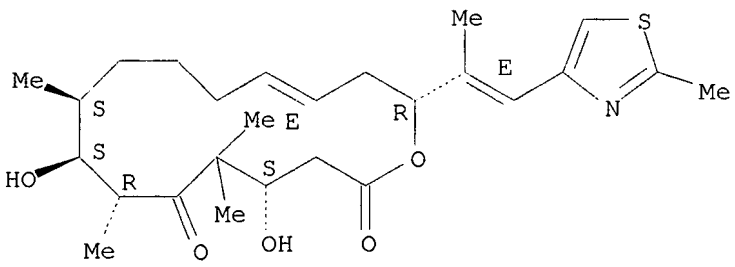
RN 198571-37-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



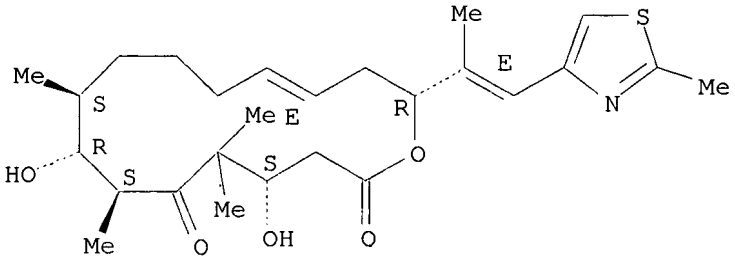
RN 198571-38-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



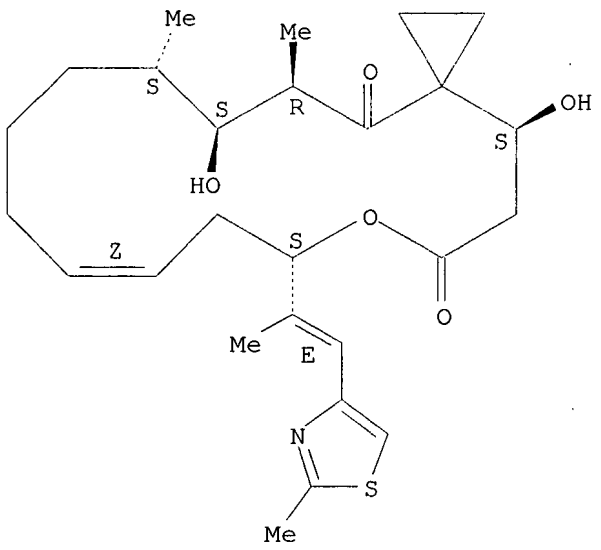
RN 198571-39-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



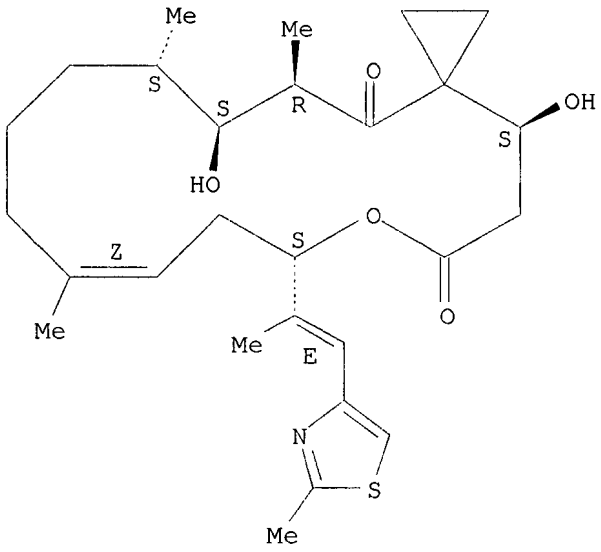
RN 198571-47-0 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,17-dimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16S,17R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



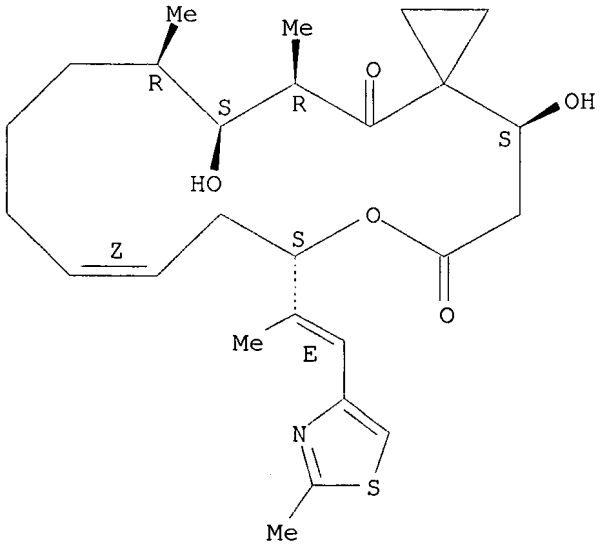
RN 198571-48-1 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-11,15,17-trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

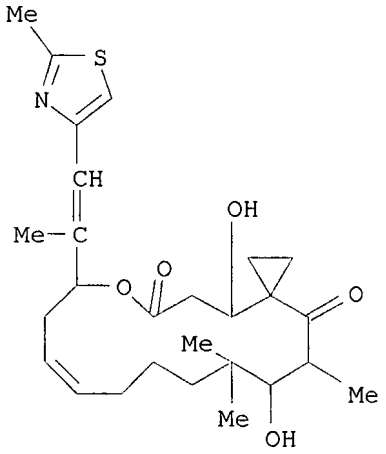


RN 198571-49-2 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,17-dimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15R,16S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



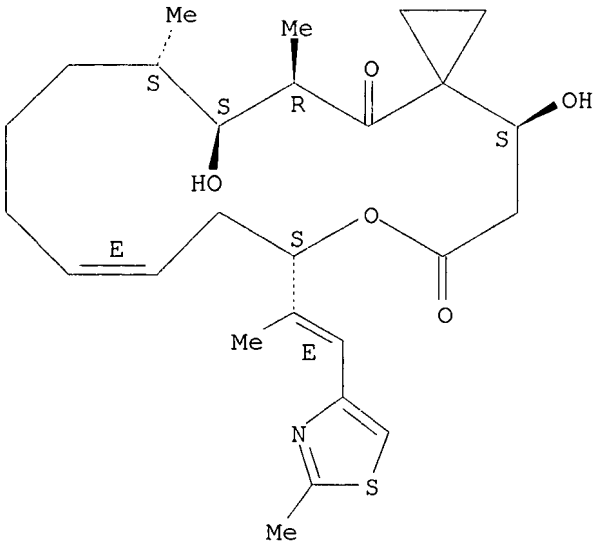
RN 198571-50-5 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,15,17-trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,16R,17R)- (9CI) (CA INDEX NAME)



RN 198571-51-6 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,17-dimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10E,15S,16S,17R)- (9CI) (CA INDEX NAME)

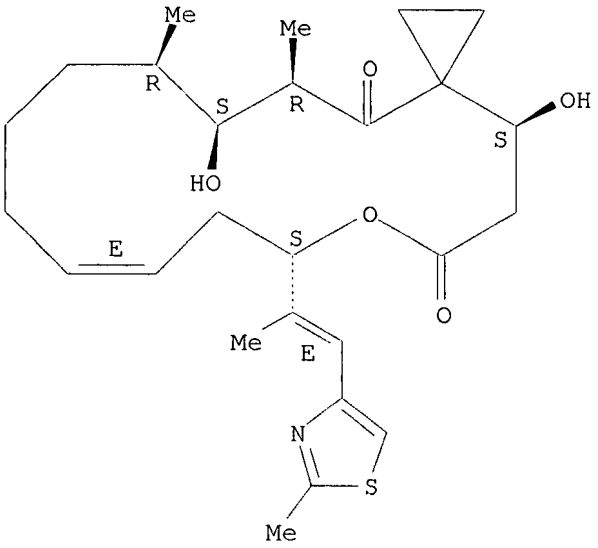
Absolute stereochemistry. Rotation (-).

Double bond geometry as described by E or Z.



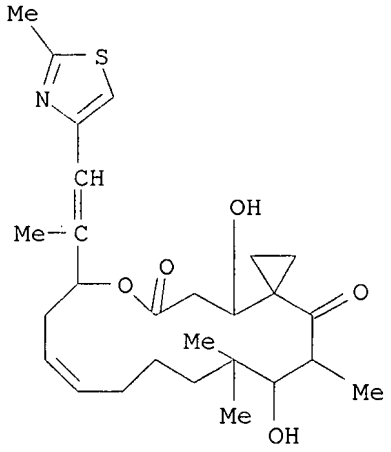
RN 198571-52-7 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10E,15R,16S,17R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



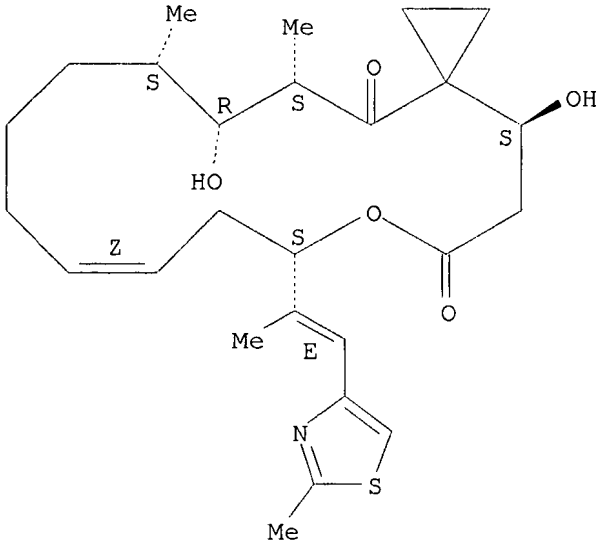
RN 198571-53-8 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,15,17-
trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,

(4S,8S,10E,16R,17R)- (9CI) (CA INDEX NAME)



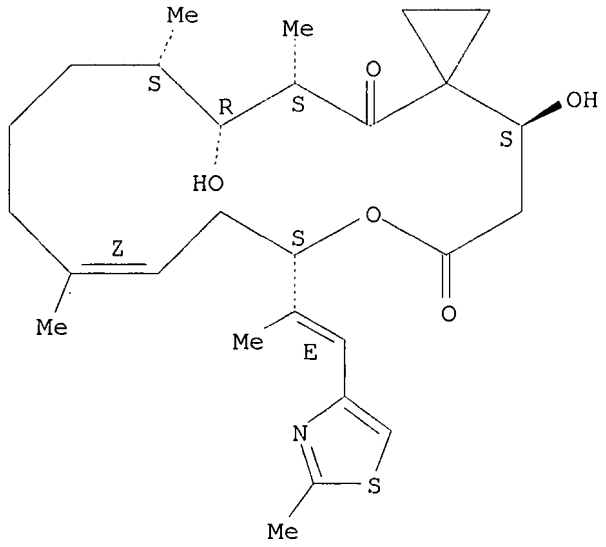
RN 198571-59-4 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,17-dimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16R,17S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



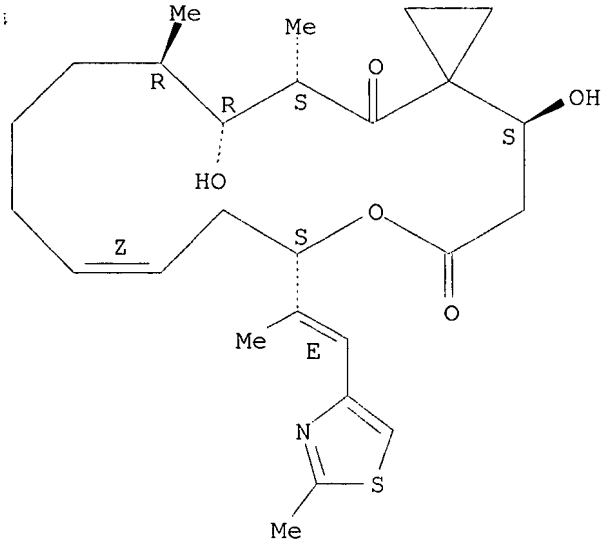
RN 198571-60-7 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-11,15,17-trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10Z,15S,16R,17S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



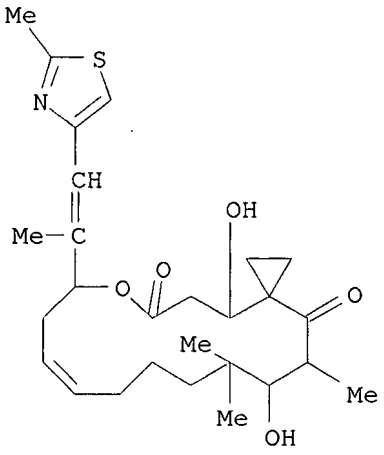
RN 198571-61-8 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10Z,15R,16R,17S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



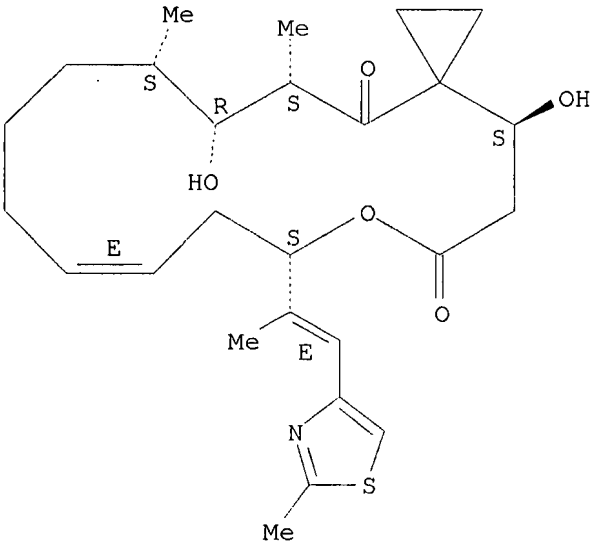
RN 198571-62-9 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,15,17-

trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10Z,16S,17S)- (9CI) (CA INDEX NAME)



RN 198571-63-0 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10E,15S,16R,17S)-
(9CI) (CA INDEX NAME)

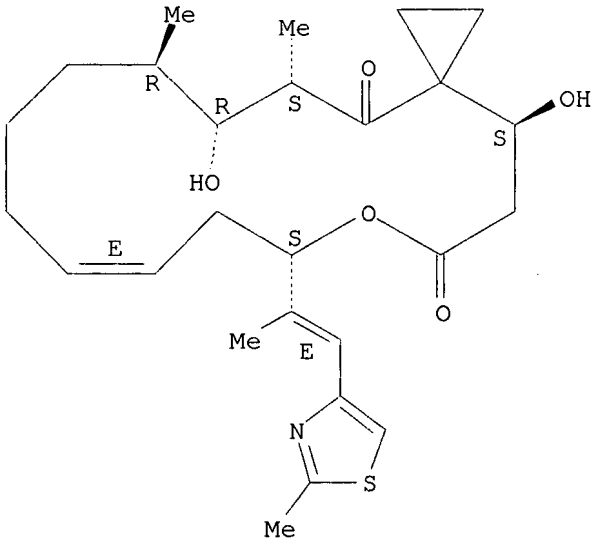
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



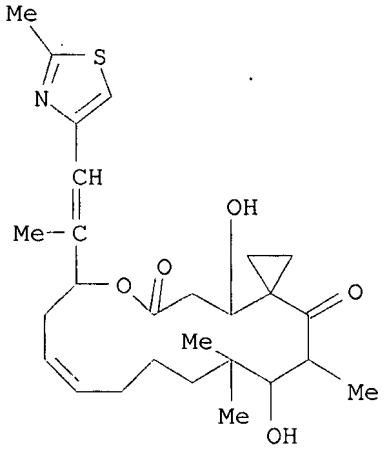
RN 198571-64-1 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione,
4,16-dihydroxy-15,17-dimethyl-8-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
(4S,8S,10E,15R,16R,17S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

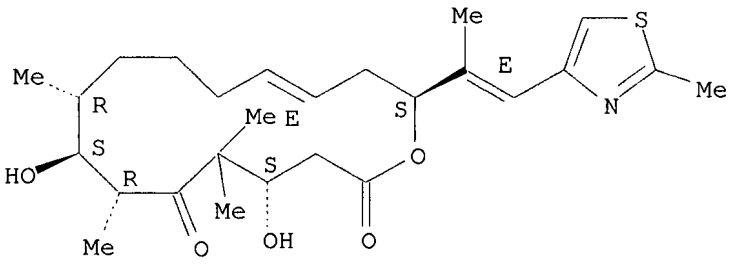


RN 198571-65-2 CAPLUS
CN 7-Oxaspiro[2.15]octadec-10-ene-6,18-dione, 4,16-dihydroxy-15,15,17-trimethyl-8-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,8S,10E,16S,17S)- (9CI) (CA INDEX NAME)



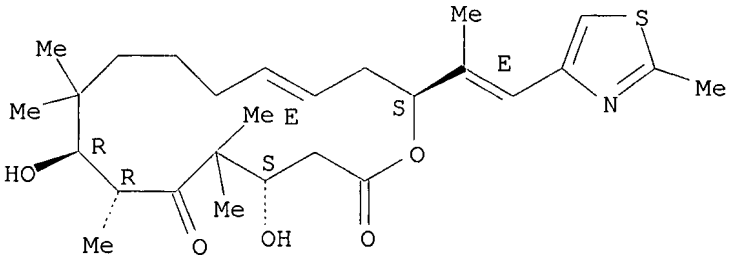
RN 198571-66-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



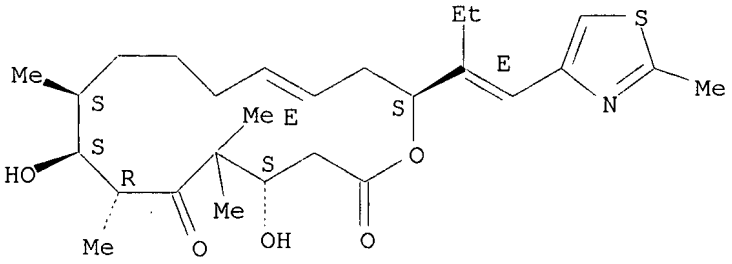
RN 198571-67-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



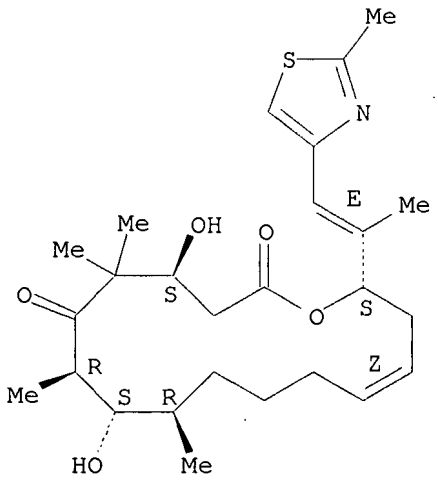
RN 198571-69-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



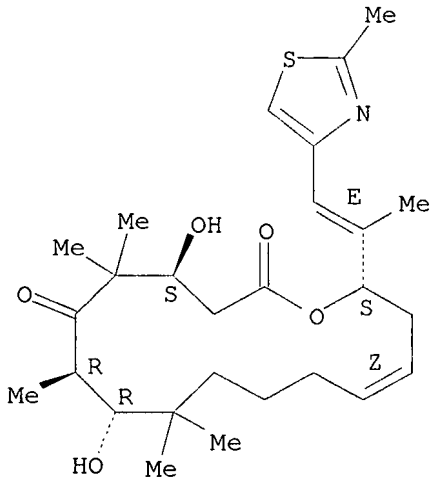
RN 198571-70-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



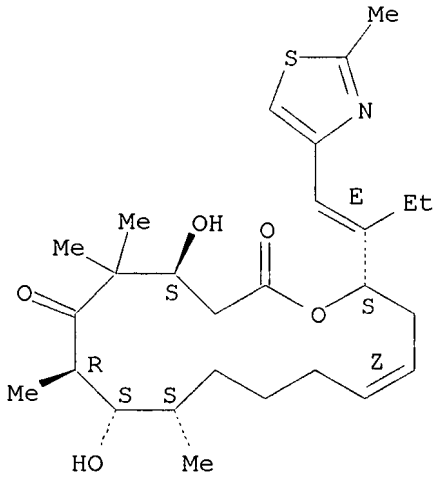
RN 198571-71-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



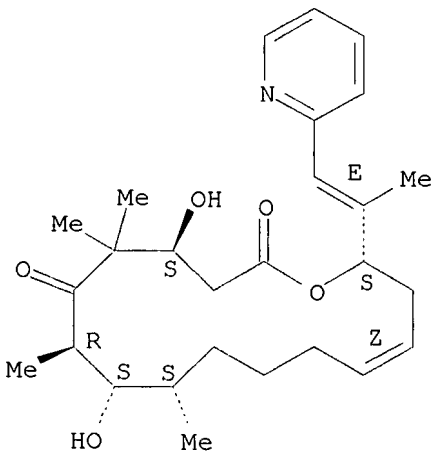
RN 198571-72-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



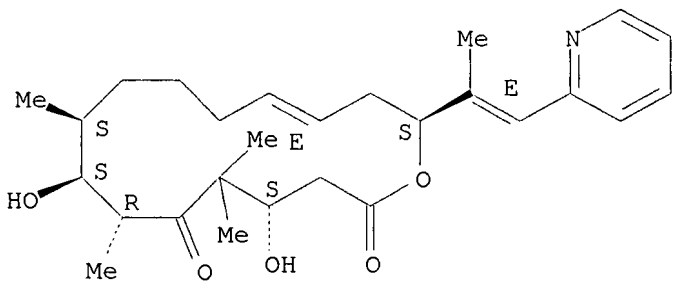
RN 198571-77-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-78-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.


Me
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OH
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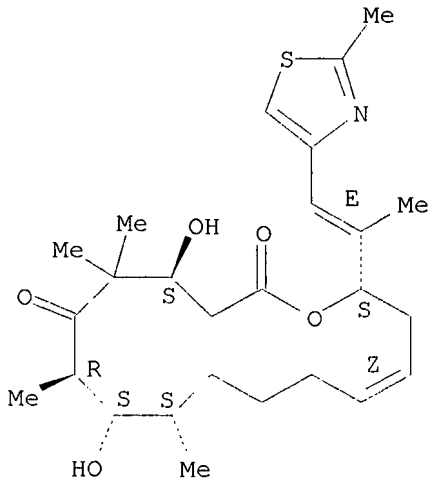
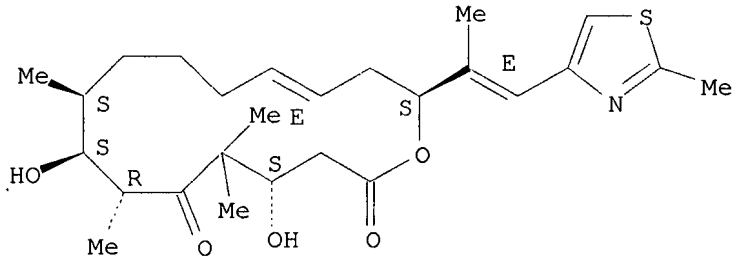
L16 ANSWER 129 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:714314 CAPLUS
DN 127:358730
TI Structure-activity relationships of the epothilones and the first in vivo comparison with paclitaxel
AU Su, Dai-Shi; Balog, Aaron; Meng, Dongfang; Bertinato, Peter; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CS Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SO Angew. Chem., Int. Ed. Engl. (1997), 36(19), 2093-2096
CODEN: ACIEAY; ISSN: 0570-0833
PB Wiley-VCH
DT Journal
LA English
AB The structure-activity relationships of the epothilones and 18 derivs. and analogs were studied. An in vivo comparison of the chemotherapeutic effect of epothilone B with that of paclitaxel was also studied. The chemotherapeutic effect of daily doses of epothilone B (0.7 mg/kg) and paclitaxel (2 mg/kg) in CB-17 SCID mice bearing drug-resistant human CCRF-CEM/VBL xenografts were T/C = 0.33 and T/C = 0.70, resp.
IT **186692-73-9**, Desoxyepothilone A **188260-10-8**
189453-10-9, Desoxyepothilone B **189453-40-5**
198475-04-6 198475-05-7 198475-06-8
198475-11-5 198475-13-7
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(structure-activity relationships of the epothilones and in vivo comparison with paclitaxel)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



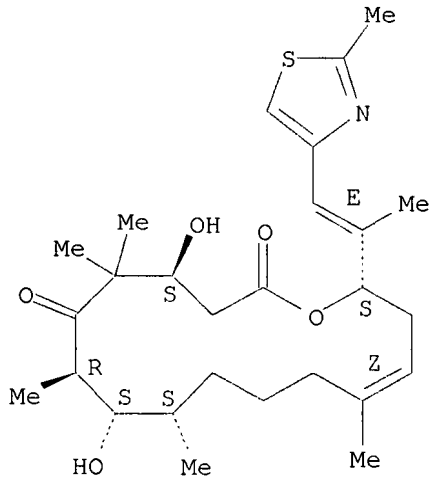
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



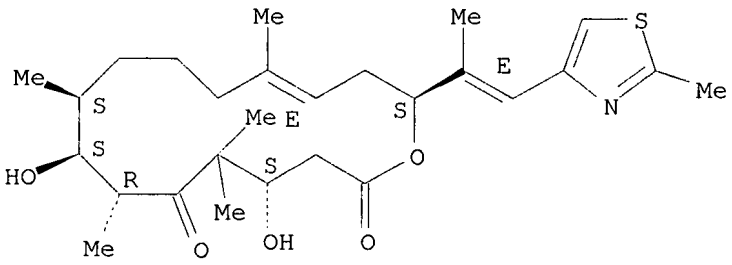
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



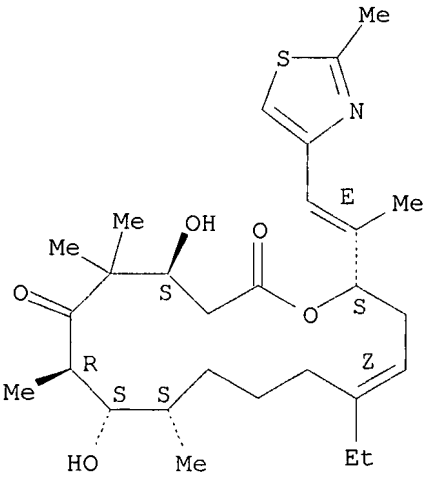
RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



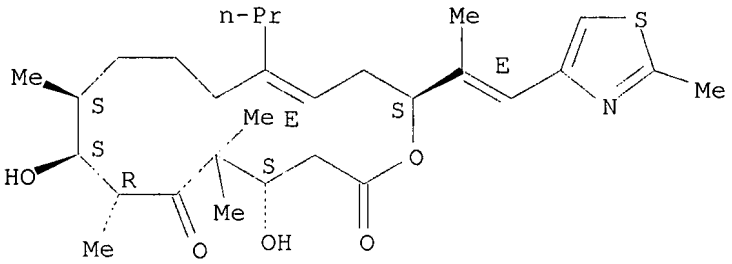
RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



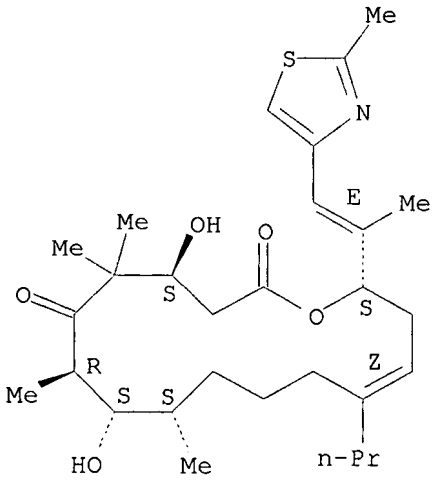
RN 198475-05-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



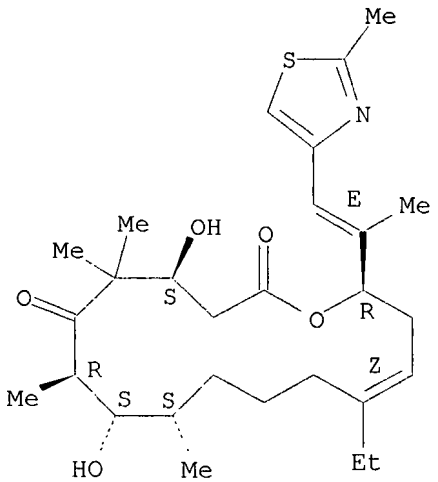
RN 198475-06-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198475-11-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

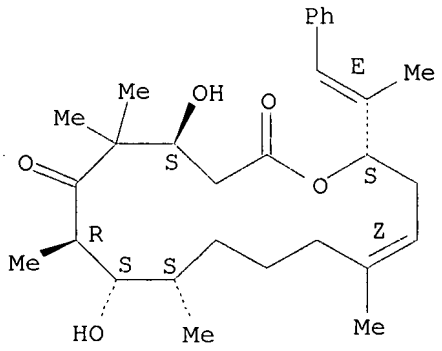
Absolute stereochemistry.
Double bond geometry as shown.



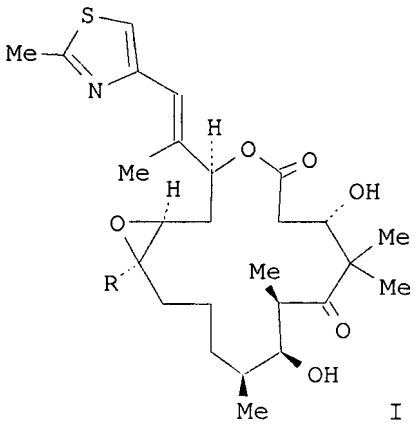
RN 198475-13-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-

[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L16 ANSWER 130 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:665094 CAPLUS
DN 127:293040
TI Total Syntheses of Epothilones A and B
AU Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Su, Dai-Shi; Kamenecka, Ted; Sorensen, Erik; Danishefsky, Samuel J.
CS Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SO J. Am. Chem. Soc. (1997), 119(42), 10073-10092
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 127:293040
GI



I

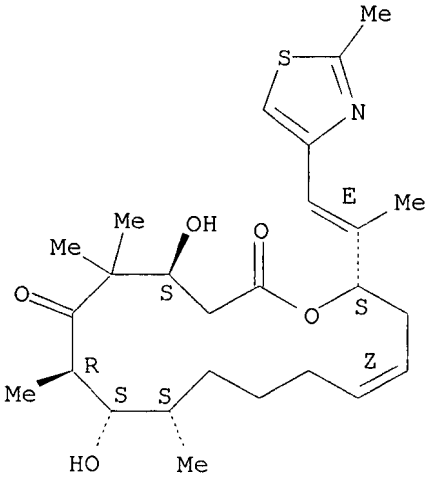
AB Convergent, stereocontrolled total syntheses of the microtubule-stabilizing macrolides epothilones A (I; R = H) and B (I; R = Me) have been achieved. Four distinct ring-forming strategies were pursued. Of these four, three were reduced to practice. In one approach, the action of a base on a substance possessing an acetate ester and a nonenolizable aldehyde brought about a remarkably effective macroaldolization simultaneously creating the C2-C3 bond and the hydroxyl-bearing stereocenter at C-3. Alternatively, the 16-membered macrolide of the epothilones could be fashioned through a C12-C13 ring-closing olefin metathesis and through macrolactonization of the appropriate hydroxy acid.
The application of a stereospecific B-alkyl Suzuki coupling strategy permitted the establishment of a cis C12-C13 olefin, thus setting the stage for an eventual site- and diastereoselective epoxidn. reaction. The development of a novel cyclopropane solvolysis strategy for incorporating the geminal Me groups of the epothilones, and the use of Lewis acid catalyzed diene-aldehyde cyclocondensation (LACDAC) and asym. allylation methodol. are also noteworthy.
IT **186692-73-9P**, (-)-Desoxyepothilone A **188259-95-2P**, 3-epi-Desoxyepothilone A **189453-10-9P**, (-)-Desoxyepothilone B
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(syntheses of epothilones A and B via macroaldolization, olefin metathesis and macrolactonization)

RN 186692-73-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

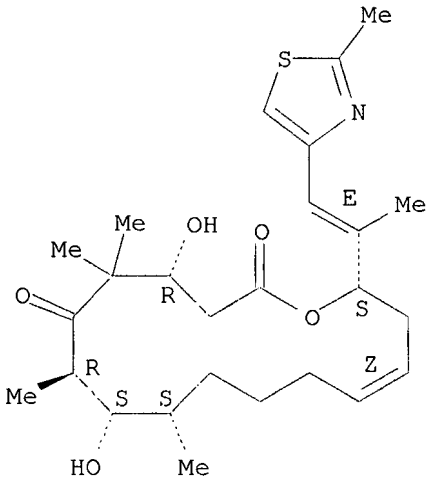
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188259-95-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

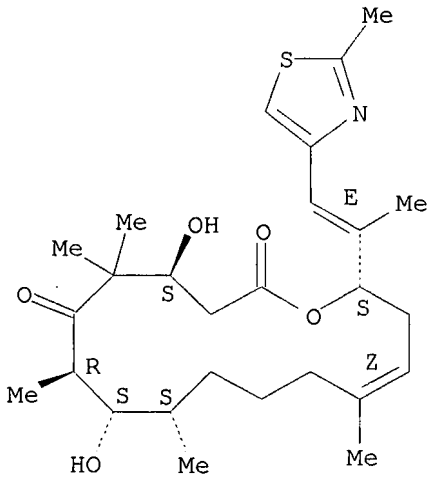
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-
(9CI) (CA INDEX NAME)

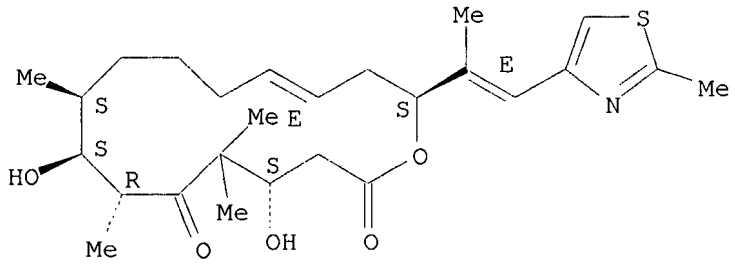
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **188260-10-8P 189453-40-5P,** (E)-Desoxyepothilone B
RL: SPN (Synthetic preparation); PREP (Preparation)
(syntheses of epothilones A and B via macroaldolization, olefin
metathesis and macrolactonization)

RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-
(9CI) (CA INDEX NAME)

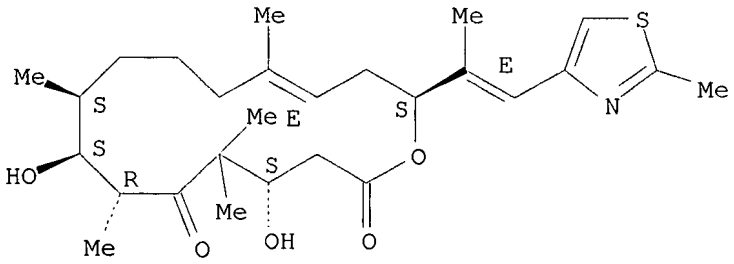
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



L16 ANSWER 131 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:528753 CAPLUS
DN 127:135660
TI Total Syntheses of Epothilones A and B via a Macrolactonization-Based Strategy
AU Nicolaou, K. C.; Ninkovic, S.; Sarabia, F.; Vourloumis, D.; He, Y.; Vallberg, H.; Finlay, M. R. V.; Yang, Z.
CS Department of Chemistry and The Skaggs, Institute for Chemical Biology, La Jolla, CA, 92037, USA
SO J. Am. Chem. Soc. (1997), 119(34), 7974-7991
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 127:135660
GI

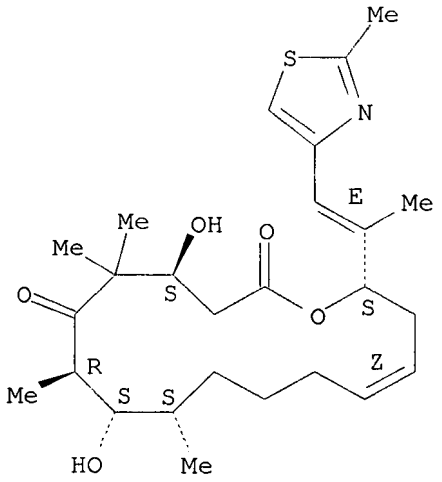
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total syntheses of epothilones A (I) (R = H) and B I (R = Me) and several analogs are described. The reported strategy relies on a macrolactonization approach and features selective epoxidn. of the macrocycle double bond in precursors II (R = H, Me) as well as high convergency and flexibility. Building blocks (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H, (S)-Me3CMe2SiOCH2CH(Me)CH2CH2CH2COR (R = H, Me), (III) [R2 = CH2CH2P+(Ph)3I-; CH2CHO] were constructed by asym. processes and coupled via Wittig, aldol, and macrolactonization reactions to afford the basic skeleton of epothilones and that of several of their analogs by a relatively short route. The utilization of intermediate III [R2 = (E)-CH2CH=C(Me)CH2CH2CH2I], obtained via a stereoselective Wittig reaction and its Enders coupling to SAMP hydrazone, in combination with a stereoselective aldol reaction with the modified substrate (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CH2OSiMe2CMe3 improved the stereoselectivity and efficiency of the total synthesis of these new and highly potent microtubule binding antitumor agents.

IT **186692-73-9P 189453-10-9P 189453-40-5P 193146-35-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total syntheses of epothilones A and B via a macrolactonization-based strategy)

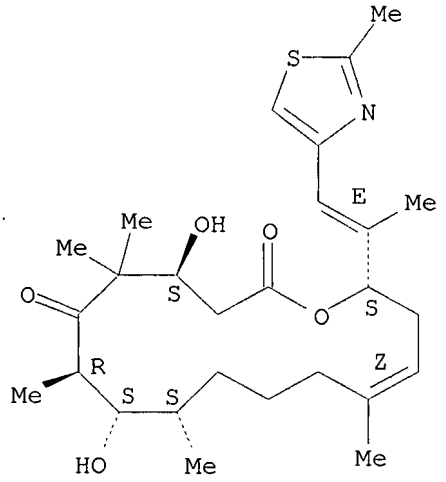
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



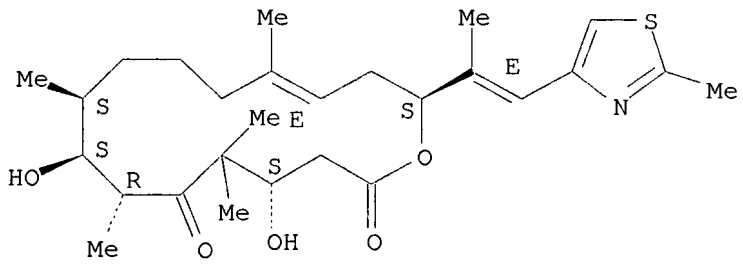
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



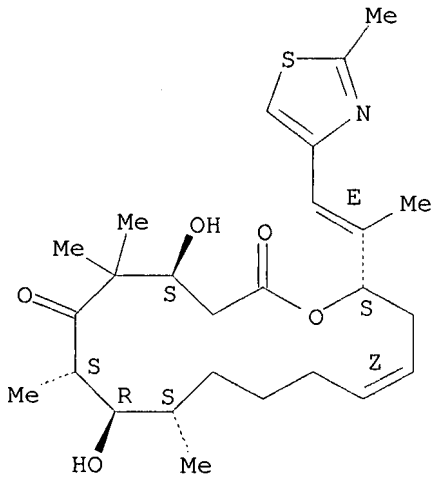
RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



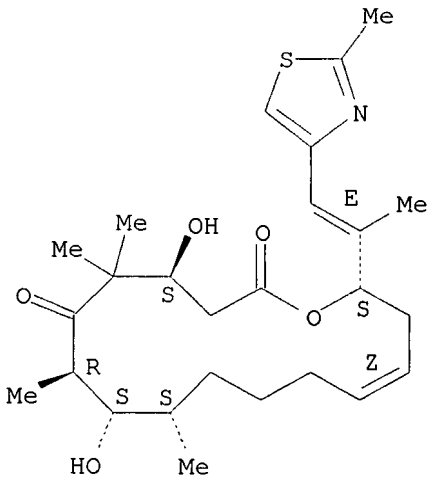
RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



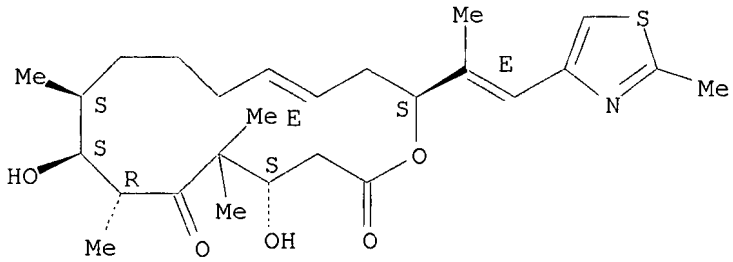
L16 ANSWER 132 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:528752 CAPLUS
DN 127:149021
TI The Olefin Metathesis Approach to Epothilone A and Its Analogs
AU Nicolaou, K. C.; He, Y.; Vourloumis, D.; Vallberg, H.; Roschangar, F.; Sarabia, F.; S.Ninkovic,; Yang, Z.; Trujillo, J. I.
CS Department of Chemistry and The Skaggs, Institute for Chemical Biology, La Jolla, CA, 92037, USA
SO J. Am. Chem. Soc. (1997), 119(34), 7960-7973
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 127:149021
GI For diagram(s), see printed CA Issue.
AB The olefin metathesis approach to epothilone A (I) and several diastereomeric analogs is described. Key building blocks II, (S)-OHCCH(Me)CH2CH2CH2CH=CH2, and (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H were constructed in optically active form and were coupled and elaborated to olefin metathesis precursor III (R = SiMe2CMe3) via an aldol reaction and an esterification coupling. Olefin metathesis of compd. III (R = SiMe2CMe3), under the catalytic influence of RuCl2(:CHPh)(PCy3)2, furnished cis- and trans-cyclic olefins IV (R = SiMe2CMe3). Epoxidn. of (Z)-IV (R = H) gave I and several analogs, whereas epoxidn. of (E)-IV (R = H) resulted in addnl. epothilones. Similar elaboration of isomeric as well as simpler intermediates resulted in yet another series of epothilone analogs and model systems.
IT **186692-73-9P 188260-10-8P 193071-86-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone A and analogs via olefin metathesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



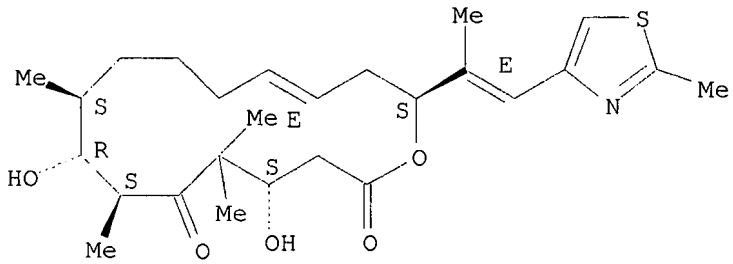
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L16 ANSWER 133 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:443365 CAPLUS
DN 127:81289
TI Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
IN Hofle, Gerhard; Kiffe, Michael
PA Gesellschaft Fur Biotechnologische Forschung Mbh (Gbf), Germany; Hofle, Gerhard; Kiffe, Michael
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9719086	A1	19970529	WO 1996-EP5080	19961118
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	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19542986	A1	19970522	DE 1995-19542986	19951117
	DE 19639456	A1	19980326	DE 1996-19639456	19960925
	EP 873341	A1	19981028	EP 1996-939097	19961118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000500757	T2	20000125	JP 1997-519381	19961118
	US 6288237	B1	20010911	US 1998-77055	19980803
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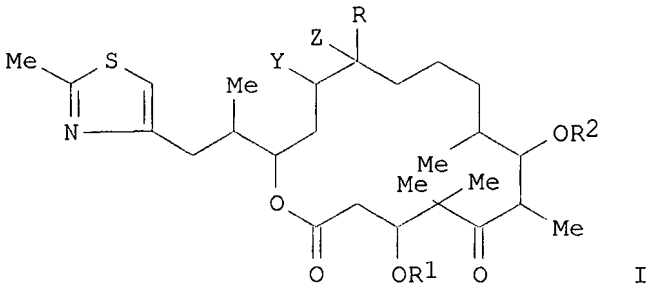
	WO 1996-EP5080	W	19961118		

OS MARPAT 127:81289
GI



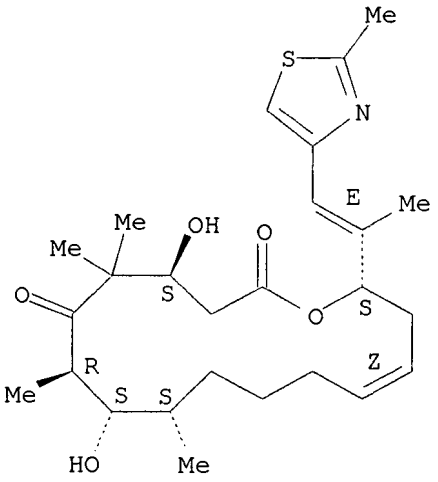
I

AB The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = H, halo, pseudohalo, OH, acyloxy, alkoxy, benzoyloxy; or YZ = O, bond; however, I may not be epothilone A or B] , useful as agrochems. and pharmaceuticals (no data), are prepd. Thus, epothilone A in acetone contg. trifluoroacetic acid was heated overnight at 50.degree. and the reaction mixt. was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP

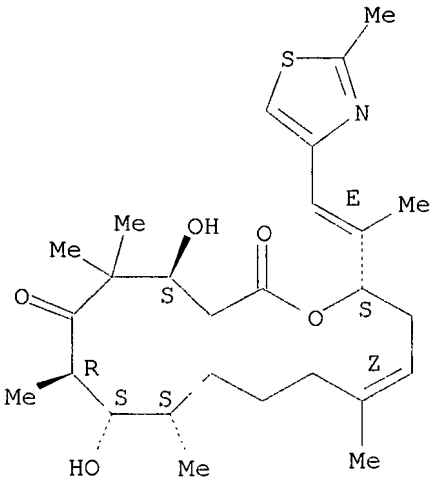
(Preparation)
(prepn. of epothilone derivs. as agrochems. and pharmaceuticals)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



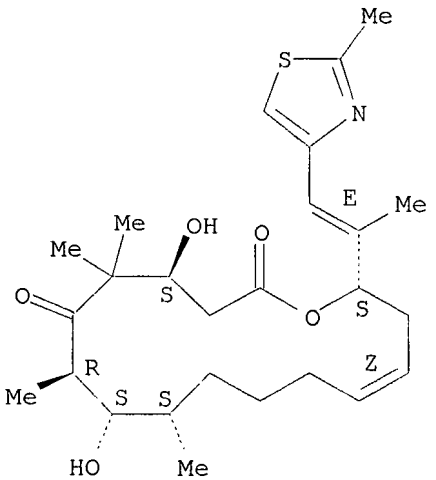
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L16 ANSWER 134 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:430309 CAPLUS
DN 127:108793
TI Stereoselective syntheses and evaluation of compounds in the 8-desmethylepothilone A series: some surprising observations regarding their chemical and biological properties
AU Balog, Aaron; Betinato, Peter; Su, Dai-Shi; Meng, Dongfang; Sorensen, Erik; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CS Lab. Bioorganic Chem., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA
SO Tetrahedron Lett. (1997), 38(26), 4529-4532
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 127:108793
AB The title compds. have been synthesized in a convergent way by recourse to
a Weiler type dianion construction.
IT **186692-73-9**, Desoxyepothilone A **189453-10-9**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(stereoselective syntheses and evaluation of compds. in the 8-desmethylepothilone A series)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

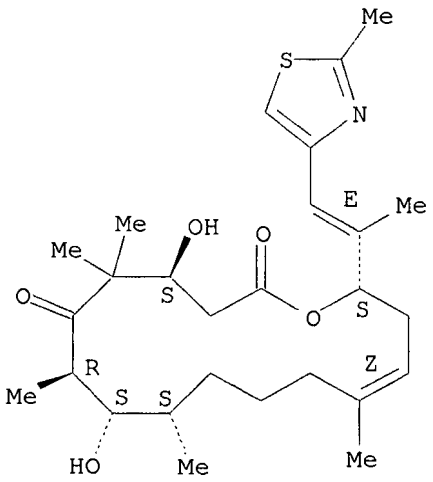
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



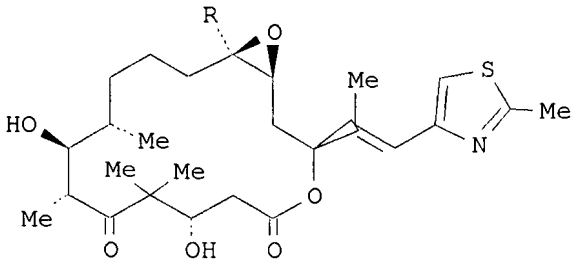
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L16 ANSWER 135 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:330310 CAPLUS
DN 127:4950
TI Synthesis of epothilones A and B in solid and solution phase
AU Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.
CS Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Nature (London) (1997), 387(6630), 268-272
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
OS CASREACT 127:4950
GI

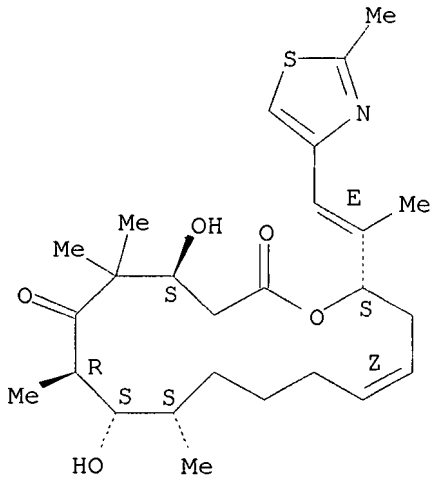


I

AB Epothilones A (I; R = H) and B (I: R = Me), two compds. that were recently isolated from myxobacterium Sorangium cellulosum strain 90, have generated intense interest among chemists, biologists and clinicians owing to the structural complexity, unusual mechanism of interaction with microtubules and anticancer potential of these mols. Like taxol, they exhibit cytotoxicity against tumor cells by inducing microtubule assembly and stabilization, even in taxol-resistant cell lines. Following the structural elucidation of these mols. by X-ray crystallog. in 1996, several synthesis of epothilones A and B have been reported, indicative of the potential importance of these mols. in the cancer field. Here we report the first solid-phase synthesis of epothilone A, the total synthesis of epothilone B, and the generation of a small epothilone library. The solid-phase synthesis applied here to epothilone A could open up new possibilities in natural-product synthesis and, together with soln.-phase synthesis of other epothilones, paves the way for the generation of large combinatorial libraries of these important mols. for biol. screening.
IT **186692-73-9P 189453-10-9P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a combinatorial library via solid-phase synthesis of epothilone A and soln.-phase synthesis of epothilone B)
RN 186692-73-9 CAPLUS

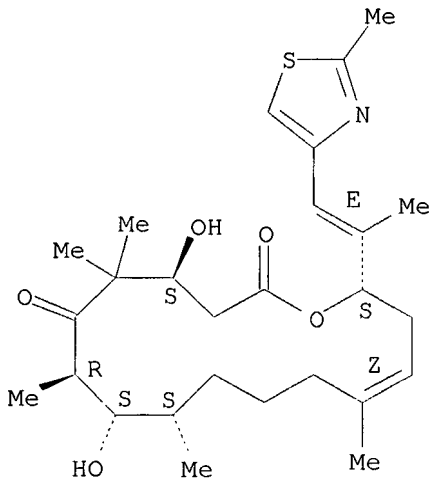
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



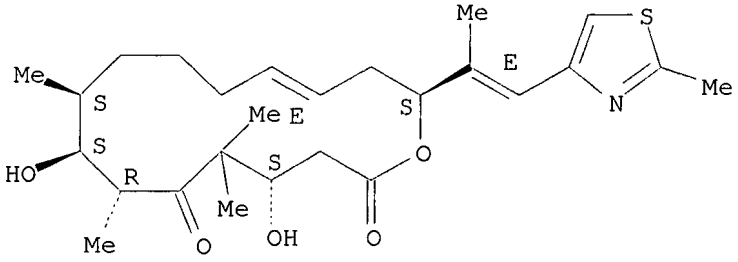
IT **188260-10-8P 189453-40-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a combinatorial library via solid-phase synthesis of

epothilone A and soln.-phase synthesis of epothilone B)

RN 188260-10-8 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

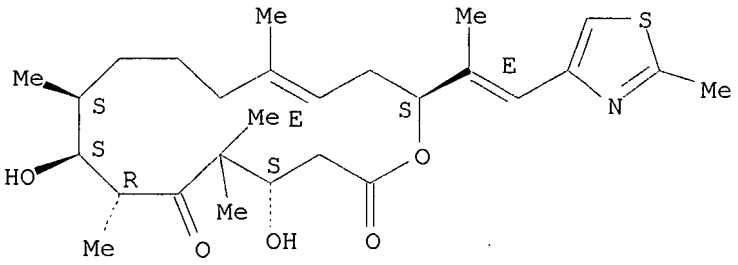
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



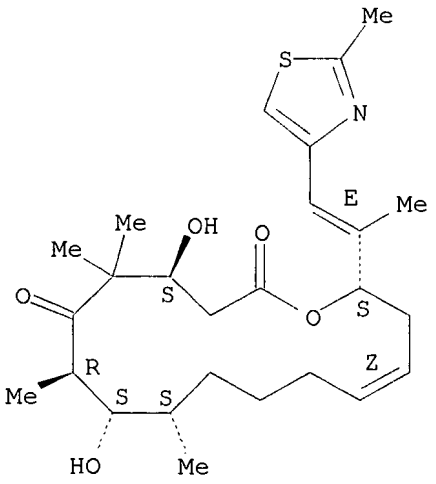
L16 ANSWER 136 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:302059 CAPLUS
DN 127:4948
TI Total synthesis of (-)-epothilone B: an extension of the Suzuki coupling method and insights into structure-activity relationships of the epothilones
AU Su, Dai-Shi; Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CS Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SO Angew. Chem., Int. Ed. Engl. (1997), 36(7), 757-759
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 127:4948
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB (-)-Epothilone B (I; R = Me, X = O) and desoxyepothilone B (I; R = Me, X = bond) were prepd. via Suzuki coupling of (Z)-vinyl iodide II with borane III. I (R = H, Me, X = O, bond) and the E-isomers of I (R = H, Me, X = bond) were tested for efficacy against drug-sensitive and resistant CCRF-CEM cell lines (IC50 = 0.0004 - 0.262 .mu.M).

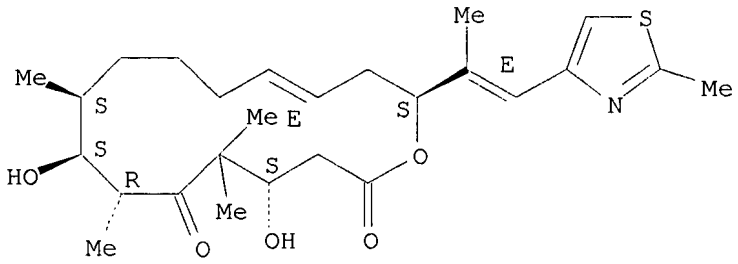
IT **186692-73-9**, Desoxyepothilone A **188260-10-8**, trans-Desoxyepothilone A **189453-40-5**, trans-Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



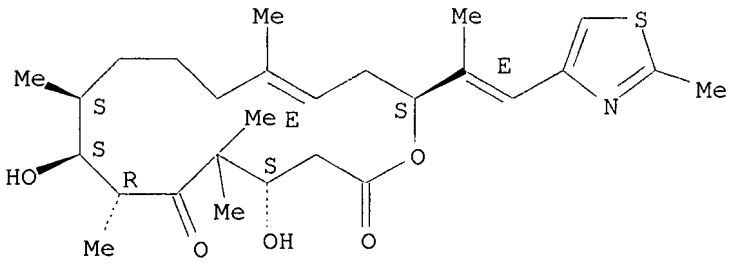
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



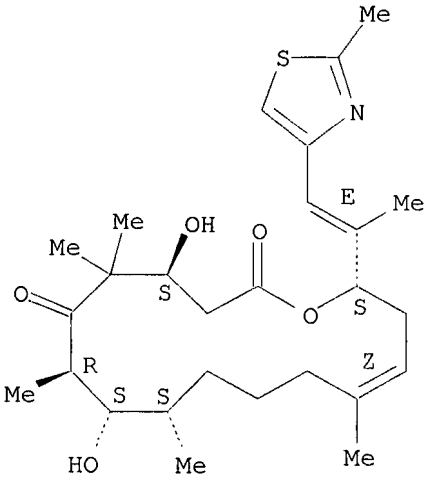
RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione,
4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

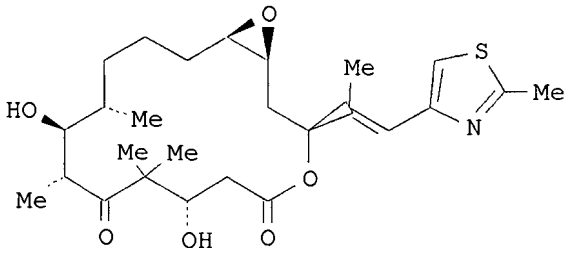


IT **189453-10-9P**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L16 ANSWER 137 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:206419 CAPLUS
DN 126:251010
TI Total synthesis of epothilone A: the macrolactonization approach
AU Nicolaou, K. C.; Sarabia, Francisco; Ninkovic, Sacha; Yang, Zhen
CS Dep. Chem., Skaggs Inst. Chem. Biol. Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Angew. Chem., Int. Ed. Engl. (1997), 36(5), 525-527
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 126:251010
GI



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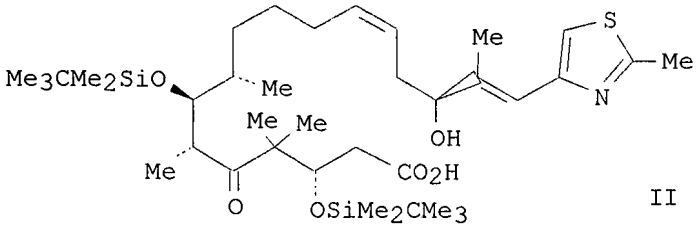
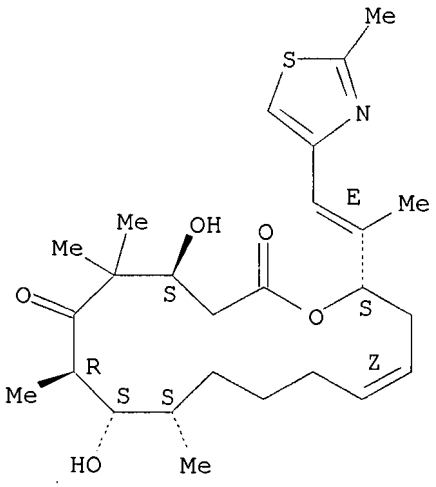


II

AB Epothilone A (I) was prepd. via a highly convergent and flexible route with macrolactonization of hydroxy acid II as the key step.

IT **186692-73-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of epothilone A via a macrolactonization approach)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.


Me
S
N
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Me
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Me
OH
O
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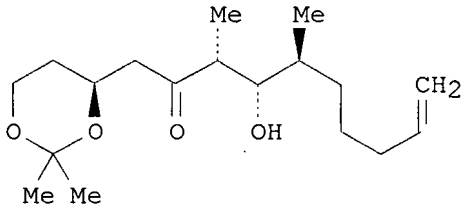
S
O
S
Z
R
Me
S
S
HO
Me

L16 ANSWER 138 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:206418 CAPLUS
DN 126:277316
TI Total synthesis of (-)-epothilone A
AU Schinzer, Dieter; Limberg, Anja; Bauer, Armin; Boehm, Oliver M.; Cordes, Martin
CS Dip. Chim., Inst. Org. Chem. Tech. Univ. Hagenring, Braunschweig, D-38106, Germany
SO Angew. Chem., Int. Ed. Engl. (1997), 36(5), 523-524
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 126:277316
GI



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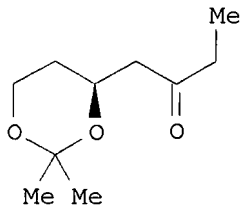
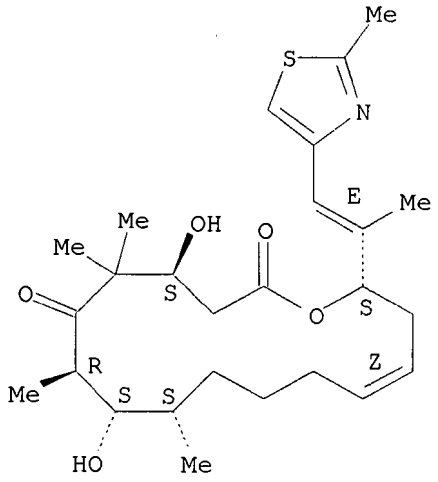


II

AB Stereoselective total synthesis of (-)-epothilone A and epothilone C was reported. The key step was the diastereoselective prepn. of intermediate ketone I by an aldol condensation of II with (S)-2-methyl-6-heptenal.

IT **186692-73-9P**, Epothilone C
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-epothilone A)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.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S
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OH
O
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S
O
S
O
R
Z
Me
S
S
HO
Me

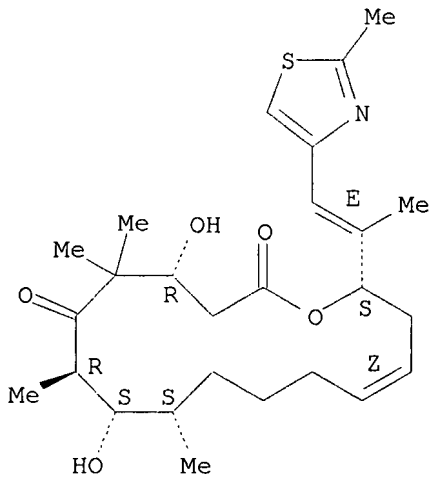
L16 ANSWER 139 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:175662 CAPLUS
DN 126:225133
TI Remote Effects in Macrolide Formation through Ring-Forming Olefin Metathesis: An Application to the Synthesis of Fully Active Epothilone Congeners
AU Meng, Dongfang; Su, Dai-Shi; Balog, Aaron; Bertinato, Peter; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CS Laboratories for Bioorganic Chemistry and Biochemical Pharmacology, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SO J. Am. Chem. Soc. (1997), 119(11), 2733-2734
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 126:225133
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A ring closing olefin metathesis strategy for the synthesis of the previously encountered desoxyepothilone A (I) is described. A merging of the alkyl segment II (carbons 12-21) and acyl segment III (carbons 3-11) through an intermol. aldol-condensation reaction provided substrates needed for ring closing olefin metathesis. Thus, thiazole IV underwent olefin metathesis in C6H6 contg. 50 mol % (PhCH:)[P(cyclohexyl)3]2RuCl2 to give 65% II and its E-isomer (Z:E 1:2). The results of these cyclization indicate a remarkable sensitivity to permutations of functionality at centers remote from the site of olefin metathesis. The in vitro biol. activity of E and Z desoxyepothilone as well as several related congeners is also described. I has IC50 range of 0.012-0.022 .mu.M against drug-sensitive and -resistant human leukemic CCRF-CEM cell lines.

IT **188259-95-2P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of antitumor epothilone congeners via ring-forming olefin metathesis)
RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

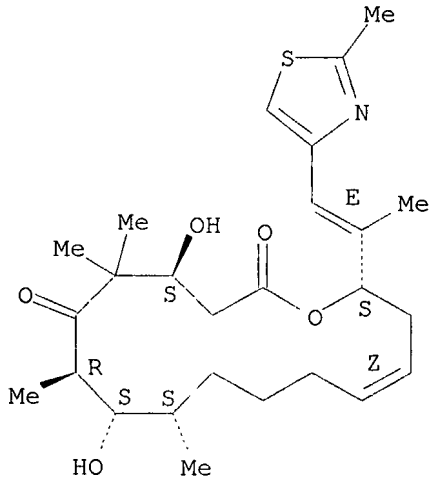


IT **186692-73-9P**, (-)-Deoxyepothilone A **188260-10-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of antitumor epothilone congeners via ring-forming olefin metathesis)

RN 186692-73-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

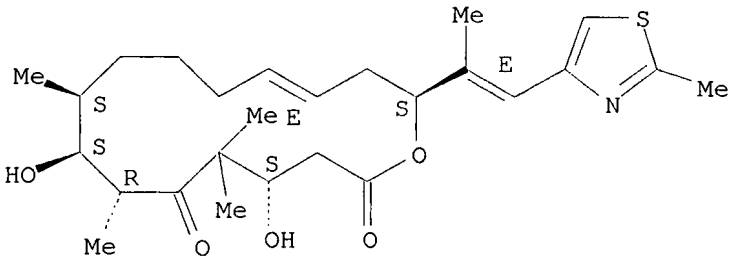
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-10-8 CAPLUS

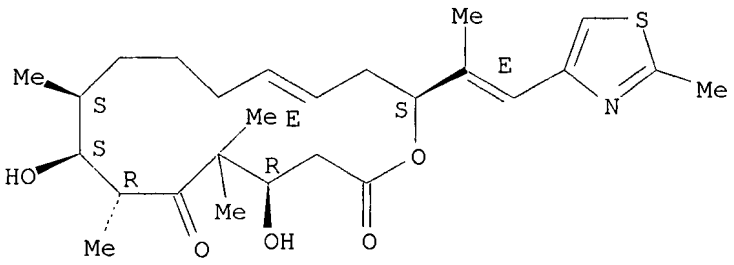
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

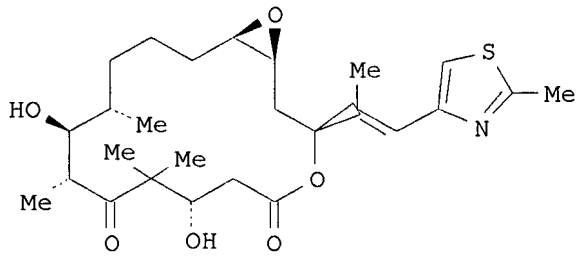


IT **188260-34-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of antitumor epothilone congeners via ring-forming olefin metathesis)
RN 188260-34-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L16 ANSWER 140 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:117381 CAPLUS
DN 126:199371
TI Total synthesis of epothilone A: the olefin metathesis approach
AU Yang, Zhen; He, Yun; Vourloumis, Dionisios; Vallberg, Hans; Nicolaou, K. C.
CS Department Chemistry Skaggs Institute Chemical Biology, Scripps Research Institute, La Jolla, CA, 92037, USA
SO Angew. Chem., Int. Ed. Engl. (1997), 36(1/2), 166-168
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 126:199371
GI



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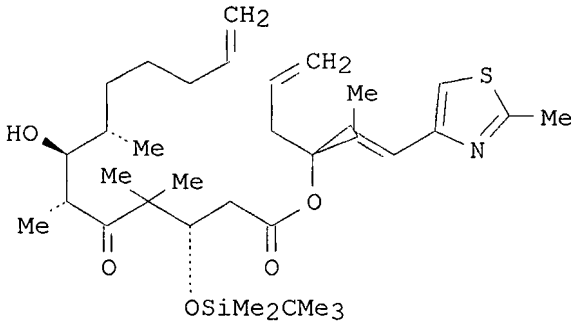
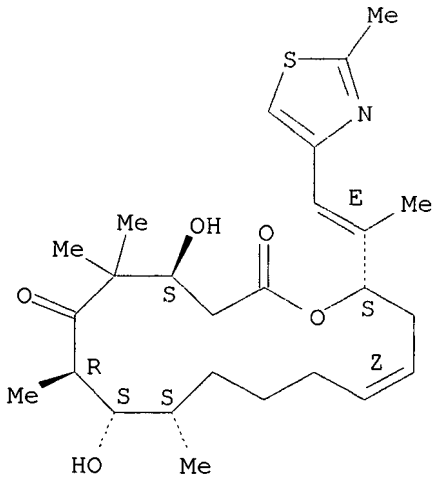


II

AB The asym. total synthesis of epothilone A (I) from EtCOCMe2CHO, (S)-H2C:CH(CH2)3CHMeCHO and Et 2-methylthiazole-4-carboxylate via metathesis of olefin II is described.

IT **186692-73-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of epothilone A via an olefin metathesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.


Me
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S
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S
R
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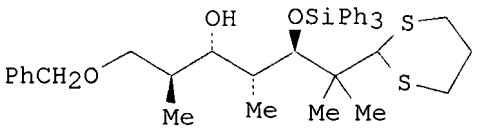
Me
S
S
HO
Me

L16 ANSWER 141 OF 141 CAPLUS COPYRIGHT 2002 ACS
AN 1997:72321 CAPLUS
DN 126:144023
TI Total synthesis of (-)-epothilone A
AU Balog, Aaron; Meng, Dongfang; Kamenecka, Ted; Bertinato, Peter; Su, Dai-Shi; Sorensen, Erik J.; Danishefsky, Samuel J.
CS Lab. for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SO Angew. Chem., Int. Ed. Engl. (1997), Volume Date 1996, 35(23/24), 2801-2803
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
GI



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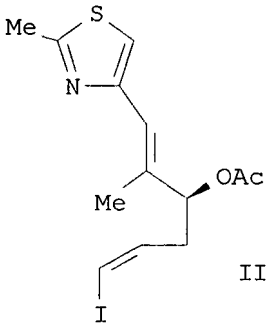
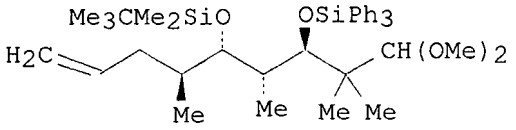


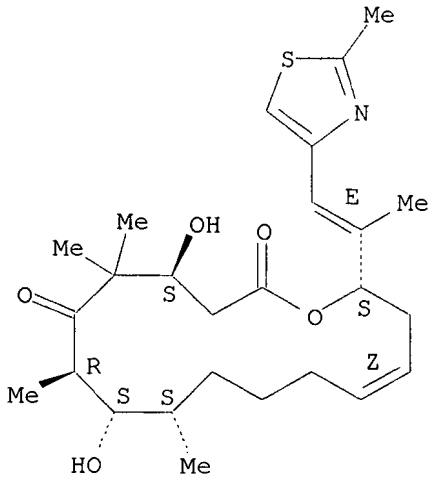
II



III

AB (-)-Epothilone A was prepd. from dithiane I, (R)-glycidol and [(2-methyl-1,3-thiazol-4-yl)methyl]diphenylphosphine oxide via a B-alkyl Suzuki coupling of thiazole II with acetal III followed by closure of the macrocycle with an aldol reaction.
IT **186692-73-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-epothilone A via a B-alkyl Suzuki coupling followed by closure of the macrocycle with an aldol reaction)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.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O
R
Z
Me
S
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HO
Me

09/084,542

=> d his

```
     (FILE 'REGISTRY' ENTERED AT 17:41:24 ON 17 MAY 2002)
                DEL HIS Y
L1              STRUCTURE UPLOADED
L2            2 S L1
L3          308 S L1 FUL
L4              STRUCTURE UPLOADED
L5            0 S L4
L6              STRUCTURE UPLOADED
L7            2 S L6

     FILE 'STNGUIDE' ENTERED AT 17:47:09 ON 17 MAY 2002

     FILE 'REGISTRY' ENTERED AT 17:48:10 ON 17 MAY 2002
L8              STRUCTURE UPLOADED
L9            1 S L8
L11          17 S L8 SAM SUB=L***
L12         300 S L8 FUL SUB=L***
L13             STRUCTURE UPLOADED
L14           0 S L13 SAM SUB=L***
L15         608 S L3 OR L12

     FILE 'CAPLUS' ENTERED AT 17:54:12 ON 17 MAY 2002
L16         141 S L15
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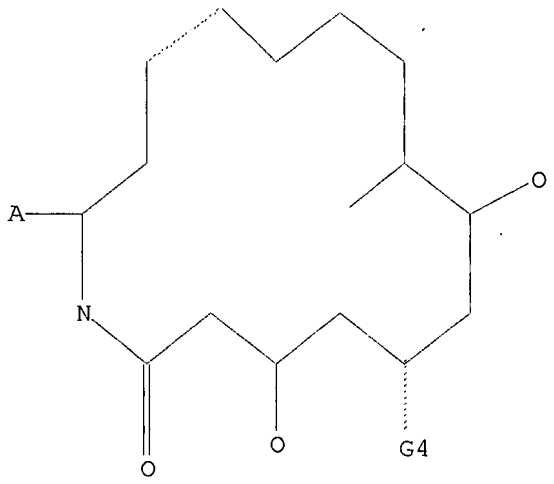
L1 STR



G1

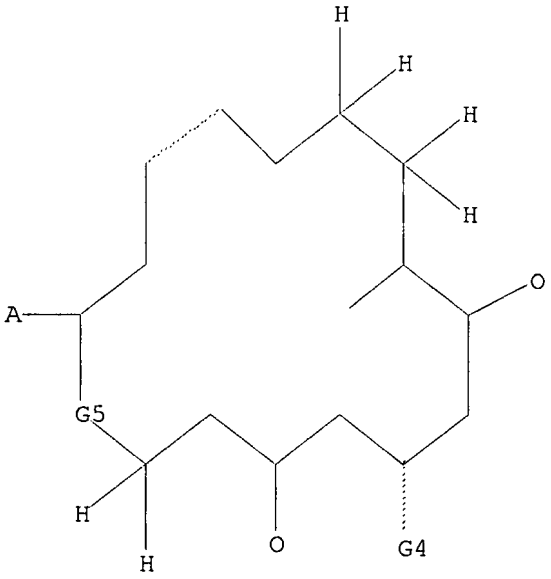
G2

G3

G4 C,H,O,N

Structure attributes must be viewed using STN Express query preparation.

L13 HAS NO ANSWERS
L13 STR



G1
G2
G3
G4 C,H,O,N
G5 O,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'REGISTRY' ENTERED AT 17:41:24 ON 17 MAY 2002)
DEL HIS Y
L1 STRUCTURE UPLOADED
L2 2 S L1
L3 308 S L1 FUL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 STRUCTURE UPLOADED
L7 2 S L6

FILE 'STNGUIDE' ENTERED AT 17:47:09 ON 17 MAY 2002

FILE 'REGISTRY' ENTERED AT 17:48:10 ON 17 MAY 2002
L8 STRUCTURE UPLOADED
L9 1 S L8
L11 17 S L8 SAM SUB=L***
L12 300 S L8 FUL SUB=L***

1/9/22
DIALOG(R)File 159:Cancerlit
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01314295 98638317
Characterization of Taxol-induced apoptosis in human prostate cancer cells (Meeting abstract).
Panvichian R; Day KC; Day ML; Pienta KJ
University of Michigan, Ann Arbor, MI 48109
Proc Annu Meet Am Assoc Cancer Res; 38:A1317 1997 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
Journal Announcement: 199801
Subfile: ICDB/98638317
Taxol, a unique antimicrotubule agent, promotes stabilization of microtubules and prevents tubulin depolymerization, thus causing G2/M cell cycle arrest as well as apoptosis. However, the molecular mechanisms of **Taxol** induced apoptosis in human cell lines is not well understood. To elucidate the relationship of cell cycle regulators and apoptosis-regulators/effectors in **Taxol** **treated** human prostate **cancer** cells, LNCaP (wild **type** P53), PC3 (mutated P53), we **treated** the cells with a continuous exposure of **Taxol** at clinically achievable concentrations and analyzed the effects at different time points. Apoptosis was confirmed by morphology and flow cytometry criteria. The protein lysate of the control and **treated** cells were analyzed by protein-SDS gel electrophoresis and Western immunoblot analysis. We demonstrate that: (1) **Taxol** produces cytotoxic effects with IC50 = 5 nM in LNCaP and 12 nM in PC3 by 48 hour exposure, (2) 90% of the PC3 cells are arrested at G2/M phase and undergo apoptosis with 40 nM **Taxol** by 24 hours of exposure, (3) Cyclin B1 and Cyclin A are unregulated during the apoptotic process, (4) Bcl-2 inactivation by phosphorylation occurs maximally at 24 hours but no changes of Bcl-x are detected. These data demonstrate that **Taxol** -induced apoptosis in prostate cancer cells is connected to cell cycle regulators independent of p53 expression.
CAS Registry No.: 0 (Antineoplastic Agents, Phytogenic); 33069-62-4 (Paclitaxel); 0 (Proto-Oncogene Proteins)

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01258843 96303554
Paclitaxel (Taxol)]
Paclitaxel **Taxol**).
Hajek R
II. interni klinika FN, Brno - Bohunice.
Cas Lek Cesk; 135(12):393-6 1996 ISSN 0008-7335 Journal Code: CPY
Languages: CZECH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English Abstract
Journal Announcement: 199610
Subfile: L MEDL/96303554
The **paclitaxel** (**TAXOL**); Bristol-Myers Squibb Company) represents first agent from novel class of antineoplastic drugs--taxanes to enter routine clinical practice. **Paclitaxel** interferes with microtubular polymerization by promoting abnormal assembly of microtubules and inhibiting their subsequent disassembly. Pharmacokinetics of **paclitaxel** has been intensively studied. There are indications for nonlinear pharmacokinetics when **paclitaxel** is administered as a short infusion and at higher doses. Neurotoxicity, mucositis, and leukopenia correlate with some pharmacokinetic parameters. The clinical development of **paclitaxel** was initially hampered by hypersensitivity reactions. Current dosage regiments with premedication reduced the incidence of these events to 3%. The major dose-limiting adverse effect of **paclitaxel** is neutropenia. Significant activities were reported especially in patients with advanced ovarian, breast, non-small cell lung cancer (NSCLC), head and neck **cancer** and in other **types** of tumours. Long-term follow-up will also allow the effects of the drug on patient survival to be determined. At present combination of **Taxol** (**paclitaxel**) with cisplatin clearly improves the duration of progression-free survival and of overall survival compared with cyclophosphamide and cisplatin in women ovarian cancer. Recently was **TAXOL** (**paclitaxel**) registered in Czech republic for **treatment** of patients with advanced metastatic ovarian carcinoma and in patients with metastatic breast cancer after failure of the standard therapy.

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01167030 95285691

Management of bladder cancer.

Raghavan D; Huben R
Department of Solid Tumor Oncology, Roswell Park Cancer Institute, State University of New York at Buffalo, USA.

Curr Probl Cancer; 19(1):1-64 1995 ISSN 0147-0272 Journal Code: DU8
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Journal Announcement: 199508
Subfile: L; M MEDL/95285691

Bladder cancer is a paradigm of malignancy, representing the spectrum from localized to metastatic disease, and manifesting varied histologic **types** , including transitional cell **carcinoma** , squamous cell carcinoma, and adenocarcinoma. Preclinical and clinical data suggest that a common stem cell of origin gives rise to the different histologic types and that these patterns are of clonal origin. Localized bladder cancer is managed optimally by transurethral resection, with or without adjuvant intravesical chemotherapy. Invasive cancer or relapsed superficial disease may require more radical surgery or radical radiotherapy. In recent years, the evolution of techniques of continent urinary diversion or of bladder replacement has revolutionized the management of invasive disease. However, the 5-year survival for invasive bladder cancer is still approximately 50%, and innovative strategies have been developed, combining definitive local **treatment** and systemic chemotherapy, in an attempt to improve survival. For patients with metastatic disease, the combination of methotrexate, vinblastine, doxorubicin, and cisplatin (the MVAC regimen) has achieved response rates as high as 70% but with a median survival of only 12 months. Until cure rates are improved, one of the hallmarks of effective management of metastatic disease will remain the provision of thorough and well-structured palliative **treatment** programs. Recently, the introduction of new agents (such as **paclitaxel** , gallium, ifosfamide, and gemcitabine) has led to promising response rates, and further clinical trials of these agents alone and in combination are in progress. In addition, an improved understanding of the mechanisms of resistance to **treatment** , including the implications of the expression of p-glycoprotein, p53 proteins, and other biochemical predictors of outcome, and of strategies to overcome such resistance, may lead to more effective management of advanced disease. Furthermore, real progress will be made only through the application of well-designed clinical trials to test the efficacy and toxicity of the new strategies of **treatment** .

Tags: Female; Human; Male
Major Descriptors: *Bladder Neoplasms
Minor Descriptors: Administration, Intravesical; Antineoplastic Agents --Administration and Dosage--AD; Antineoplastic Agents, Combined --Therapeutic Use--TU; Bladder Neoplasms--Etiology--ET; Bladder Neoplasms --Mortality--MO; Bladder Neoplasms--Therapy--TH; BCG Vaccine--Therapeutic Use--TU; Combined Modality Therapy; Cystectomy; Radiotherapy Dosage; Survival Rate; Urinary Diversion
CAS Registry No.: 0 (Antineoplastic Agents); 0 (Antineoplastic Agents, Combined); 0 (BCG Vaccine)

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DIALOG(R)File 159:Cancerlit
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00944126 92354022

Combined antimicrotubule activity of estramustine and taxol in human prostatic carcinoma cell lines.

Speicher LA; Barone L; Tew KD
Department of Pharmacology, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111.

Cancer Res; 52(16):4433-40 1992 ISSN 0008-5472 Journal Code: CNF
Contract/Grant No.: 5R01 CA 43783-07, CA, NCI; CA-09035-16, CA, NCI
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 199210
Subfile: L; M; X MEDL/92354022

Estramustine (EM) and **taxol** , two antimicrotubule agents with distinct and apparently opposing mechanisms of action, were found to be effective in combination in the preclinical **treatment** of EM-resistant and sensitive, wild- **type** human prostatic **carcinoma** cell lines. Estramustine combined with 1 nM **taxol** (concentration 100-fold less than that measured in plasma of patients **treated** with **taxol**) produced greater than additive effects on the inhibition of cell survival of both wild-type and EM-resistant cells. When **taxol** was used with another microtubule-destabilizing drug, vinblastine, no significantly increased cytotoxicity was observed. Other effects on wild-type and EM-resistant cells produced by the combination of EM and **taxol** included (a) an increased proportion of the cells in the S phase of the cell cycle; (b) no mitotic block; and (c) an increase in the percentage of micronucleated cells from a control value of less than 1% to greater than 20% after drug **treatment** . Immunofluorescent microscopic analysis of the effect of this drug combination on the mitotic spindle apparatus revealed specific examples of aberrant mitotic figures, including multiple asters, cells with two distinct spindles, and tripolar spindles able to traverse mitosis and complete cytokinesis. These data provide supportive preclinical evidence for the potential development of an EM/ **taxol** combination clinical regimen either for prostate or other cancers.

Tags: Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Major Descriptors: *Antineoplastic Agents, Combined--Pharmacology--PD; *Carcinoma--Drug Therapy--DT; *Microtubules--Drug Effects--DE; *Prostatic Neoplasms--Drug Therapy--DT
Minor Descriptors: Alkaloids--Pharmacology--PD; Antineoplastic Agents, Phytogenic--Pharmacology--PD; Carcinoma--Ultrastructure--UL; Cell Cycle --Drug Effects--DE; Drug Screening Assays, Antitumor; Estramustine --Pharmacology--PD; Flow Cytometry; Micronucleus Tests; Microtubules --Ultrastructure--UL; Prostatic Neoplasms--Ultrastructure--UL; Tumor Cells, Cultured; Tumor Stem Cell Assay
CAS Registry No.: 0 (Alkaloids); 0 (Antineoplastic Agents, Combined); 0 (Antineoplastic Agents, Phytogenic); 2998-57-4 (Estramustine); 33069-62-4 (Paclitaxel)

1/9/29
DIALOG(R)File 159:Cancerlit
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01123693 95136888

Paclitaxel . **A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in the** treatment **of cancer.**

Spencer CM; Faulds D
Adis International Limited, Auckland, New Zealand.

Drugs; 48(5):794-847 1994 ISSN 0012-6667 Journal Code: EC2
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC
Journal Announcement: 199504
Subfile: L; M MEDL/95136888

Paclitaxel is a new anticancer agent with a novel mechanism of action. It promotes polymerisation of tubulin dimers to form microtubules and stabilises microtubules by preventing depolymerisation. In noncomparative trials, continuous infusion of **paclitaxel** 110 to 300 mg/m2 over 3 to 96 hours every 3 to 4 weeks produced a complete or partial response in 16 to 48% of patients with ovarian cancer and 25 to 61.5% of patients with metastatic breast cancer, many of whom were refractory to **treatment** with cisplatin or doxorubicin, respectively. 23 to 100% of patients with ovarian cancer achieved complete or partial responses with **paclitaxel** in combination with cisplatin, carboplatin, cyclophosphamide, altretamine and/or doxorubicin. Similarly, response rates of 30 to 100% were observed with **paclitaxel** plus doxorubicin, cisplatin, mitoxantrone and/or cyclophosphamide in patients with metastatic breast cancer. Comparative trials in patients with advanced ovarian cancer showed **paclitaxel** therapy to produce greater response rates than **treatment** with parenteral hydroxyurea (71 vs 0%) or cyclophosphamide (when both agents were combined with cisplatin) [79 vs 63%]. **Paclitaxel** was also more effective than mitomycin in 50 patients with previously untreated breast cancer (partial response in 20 vs 4% of patients). **Paclitaxel** therapy also produced promising results in patients with advanced squamous cell carcinoma of the head and neck, malignant melanoma, advanced non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), germ cell cancer, urothelial cancer, oesophageal cancer, non-Hodgkin's lymphoma or multiple myeloma, and was successfully combined with cisplatin, carboplatin and/or etoposide in patients with NSCLC, SCLC or advanced squamous cell carcinoma of the head and neck. Hypersensitivity reactions were initially a concern with administration of **paclitaxel** , although current dosage regimens have reduced the incidence of these events to less than 5%. The major dose-limiting adverse effects of **paclitaxel** are leucopenia (neutropenia) and peripheral neuropathy. Other haematological toxicity was generally mild. Cardiac toxicity was reported in small numbers of patients and most patients developed total alopecia. Several aspects of **paclitaxel** use remain to be clarified, including the optimal **treatment** schedule and infusion time, confirmation of the tolerability profile and efficacy of combination regimens in an expanded range of malignancies. Long term follow-up of **paclitaxel** recipients will also allow the effects of the drug on patient survival to be determined. Nevertheless, **paclitaxel** is a promising addition to the current therapies available, with significant activity reported in patients with advanced ovarian or breast **cancer** or other **types** of tumors.(ABSTRACT TRUNCATED AT 400 WORDS)

Tags: Animal; Human
Major Descriptors: Antineoplastic Agents--Pharmacology--PD; *Antineoplastic Agents--Therapeutic Use--TU; *Neoplasms--Drug Therapy--DT; * **Paclitaxel** --Pharmacology--PD; **Paclitaxel** --Therapeutic Use--TU
Minor Descriptors: Antineoplastic Agents--Pharmacokinetics--PK; Clinical Trials; **Paclitaxel** --Pharmacokinetics--PK
CAS Registry No.: 0 (Antineoplastic Agents); 33069-62-4 (Paclitaxel)

3/9/4
DIALOG(R)File 159:Cancerlit
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01653995 20546132

Novel chemotherapeutic agents for the treatment of brain cancer.

Newton HB

Department of Neurology, The Ohio State University Hospitals, 465 Means Hall, 1654 Upham Drive, Columbus, Ohio 43210, USA. newton.12@osu.edu

Expert Opin Investig Drugs; 9(12):2815-29 2000 ISSN 1354-3784
Journal Code: DUM
Contract/Grant No.: CA16058, CA, NCI
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Journal Announcement: 200102
Subfile: L; I MEDL/20546132

Brain cancer encompasses both primary and metastatic brain tumours and accounts for over 120,000 new patients each year. Despite aggressive therapy, the majority of patients with brain cancer have poor prognosis and have brief survival intervals. Current chemotherapy drugs, used alone or in combination, have minimal or only modest activity. Novel agents that have recently been applied to **brain** cancer include temozolomide, irinotecan and **paclitaxel** . Temozolomide is a DNA alkylating agent, irinotecan inhibits DNA topoisomerase I and paclitaxel binds to microtubules and induces polymerisation. Neoplastic angiogenesis and brain tumour invasion are also targets for therapeutic intervention with new agents such as thalidomide, suramin and marimastat. All of these agents have demonstrated activity against brain cancer in vitro. Several of the drugs, in particular temozolomide, paclitaxel and irinotecan, have entered preliminary clinical trials and have demonstrated some efficacy. However, chemotherapy for primary brain tumours remains rather non-specific and mostly ineffective. The use of chemotherapy may be more effective against selected metastatic brain tumours. Continued basic research is needed to further elucidate the genetic basis of transformation, tumour invasion and angiogenesis. It is hoped that this research will lead to new therapeutic targets for drug design and development. In addition, new strategies must be developed to overcome the problem of chemotherapy resistance.

Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Major Descriptors: *Antineoplastic Agents--Therapeutic Use--TU; *Brain Neoplasms--Drug Therapy--DT
Minor Descriptors: Brain Neoplasms--Pathology--PA
CAS Registry No.: 0 (Antineoplastic Agents)

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DIALOG(R)File 159:Cancerlit
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01675462 21104159

Phase I trial of escalating doses of paclitaxel combined with fixed doses of cisplatin and doxorubicin in advanced endometrial cancer and other gynecologic malignancies: a Gynecologic Oncology Group study.

Fleming GF; Fowler JM; Waggoner SE; Copeland LJ; Greer BE; Horowitz I; Sutton G; Schilder RJ; Fracasso PM; Ball HG; McGuire WP 3rd

Department of Medicine, Division of Gynecologic Oncology, University of Chicago, Chicago, IL, USA.

J Clin Oncol; 19(4):1021-9 2001 ISSN 0732-183X Journal Code: JCO

Contract/Grant No.: CA 27469, CA, NCI; CA 37517, CA, NCI

Languages: ENGLISH

Document Type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE I; JOURNAL ARTICLE

Journal Announcement: 200104

Subfile: L; I MEDL/21104159

PURPOSE: The primary objective of this phase I trial was to determine the feasibility of administering a combination of paclitaxel, cisplatin, and doxorubicin with or without granulocyte colony-stimulating factor (G-CSF) in patients with advanced endometrial and other gynecologic cancers. PATIENTS AND METHODS: Patients were chemotherapy-naive. Doxorubicin was administered as a brief infusion, paclitaxel for 3 hours, and cisplatin for 60 minutes. Treatments were repeated every 3 weeks. For most dose levels, the cisplatin and doxorubicin were fixed at 60 mg/m(2) and 45 mg/m(2), whereas the paclitaxel was escalated in successive cohorts from 90 to 250 mg/m(2). Patients who had received previous radiotherapy to the whole pelvis were escalated separately from those who had not. RESULTS: Eighty patients received 320 cycles of therapy. When G-CSF was not used, myelosuppression prevented escalation beyond the starting dose for patients with or without previous pelvic radiotherapy. When G-CSF was added, neurotoxicity became dose-limiting for both groups. Ten patients were removed from the study for asymptomatic declines in ejection fraction, but no symptomatic congestive heart failure was observed. Major antitumor responses occurred in 46% of patients (six of 13) with measurable endometrial carcinoma and 50% of patients (eight of 16) with measurable **cervical** carcinoma. CONCLUSION: The combination of **paclitaxel**, doxorubicin, and cisplatin at relevant single-agent doses is active and feasible with the addition of G-CSF. A regimen of cisplatin 60 mg/m(2), doxorubicin 45 mg/m(2), and paclitaxel 160 mg/m(2) with G-CSF support is recommended for further testing.

Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.

Major Descriptors: *Antineoplastic Agents, Combined--Therapeutic Use--TU; *Endometrial Neoplasms--Drug Therapy--DT; *Genital Neoplasms, Female--Drug Therapy--DT

Minor Descriptors: Adult; Aged; Bone Marrow--Drug Effects--DE; Cisplatin --Administration and Dosage--AD; Cisplatin--Adverse Effects--AE; Doxorubicin--Administration and Dosage--AD; Doxorubicin--Adverse Effects --AE; Drug Administration Schedule; Feasibility Studies; Granulocyte Colony-Stimulating Factor--Administration and Dosage--AD; Granulocyte Colony-Stimulating Factor--Adverse Effects--AE; Heart--Drug Effects--DE; Middle Age; Paclitaxel--Administration and Dosage--AD; Paclitaxel--Adverse Effects--AE; Peripheral Nerves--Drug Effects--DE

CAS Registry No.: 0 (Antineoplastic Agents, Combined); 143011-72-7 (Granulocyte Colony-Stimulating Factor); 15663-27-1 (Cisplatin); 23214-92-8 (Doxorubicin); 33069-62-4 (Paclitaxel)

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01326325 97198993

The development and clinical utility of the taxane class of antimicrotubule chemotherapy agents.

Rowinsky EK

Cancer Therapy and Research Center, Institute for Drug Development, San Antonio, Texas 78229, USA.

Annu Rev Med; 48:353-74 1997 ISSN 0066-4219 Journal Code: 6DR

Languages: ENGLISH

Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

Journal Announcement: 199706

Subfile: L; M MEDL/97198993

The taxane class of antimicrotubule anticancer agents is perhaps the most important addition to the chemotherapeutic armamentarium against cancer over the past several decades. After only a brief period, the taxanes have not only demonstrated a unique ability to palliate the symptoms of many **types** of advanced **cancers** , including carcinoma of the ovary, lung, head and neck, bladder, and esophagus, they have also demonstrated effectiveness in the initial therapy of earlier stages of cancer, a setting in which any new therapy is likely to make its greatest impact. The challenge now facing investigators is to develop strategies to maximize therapeutic benefits with the taxanes in the early stages, as well as the advanced stages, of many cancers. This review describes the preclinical features and clinical results of the two major taxanes, **paclitaxel** (**Taxol** , Bristol-Myers Squibb) and docetaxel (Taxotere, Rhone-Poulenc Rhorer).

Tags: Animal; Human

Major Descriptors: Antineoplastic Agents, Phytogenic--Therapeutic Use--TU ; *Microtubules--Drug Effects--DE; *Neoplasms--Drug Therapy--DT; * **Paclitaxel** --Analogs and Derivatives--AA; ***Paclitaxel** --Therapeutic Use --TU

Minor Descriptors: Antineoplastic Agents, Phytogenic--Adverse Effects--AE ; Clinical Trials; **Paclitaxel** --Adverse Effects--AE; **Treatment** Outcome

CAS Registry No.: 0 (Antineoplastic Agents, Phytogenic); 114977-28-5 (docetaxel); 33069-62-4 (Paclitaxel)

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01383157 98037561

Synergistic inhibition of growth and induction of apoptosis by 8-chloro-cAMP and paclitaxel or cisplatin in human cancer cells.

Tortora G; di Isernia G; Sandomenico C; Bianco R; Pomatico G; Pepe S; Bianco AR; Ciardiello F

Dipartimento di Endocrinologia e Oncologia Molecolare e Clinica, Facolta di Medicina e Chirurgia, Universita degli Studi di Napoli Federico II, Naples, Italy.

Cancer Res; 57(22):5107-11 1997 ISSN 0008-5472 Journal Code: CNF

Languages: ENGLISH

Document Type: JOURNAL ARTICLE

Journal Announcement: 199801

Subfile: L; M; X MEDL/98037561

8-Chloro-cAMP (8-Cl-cAMP) is a novel agent that is able to inhibit the growth of a wide variety of **cancer** cell **types** in vitro and in vivo and, at doses devoid of toxicity, to achieve plasma concentrations in cancer patients in a range effective for cancer cell growth inhibition. In this study, we have demonstrated that 8-Cl-cAMP, at a dose causing mild or no growth inhibition, synergistically increased the growth-inhibitory effect of **paclitaxel** or cisplatin in a wide series of cell lines including human breast, lung, ovary, colon, and head carcinomas and melanoma. A similar effect was also observed with another taxane, docetaxel, and with the platinum-derivative carboplatin. 8-Cl-cAMP also markedly enhanced apoptotic cell death induced by each cytotoxic drug. A cooperative antitumor effect was also observed in vivo, because **treatment** with **paclitaxel** followed by 8-Cl-cAMP markedly inhibited the growth of GEO human colon cancer xenografts as compared to **paclitaxel** alone without signs of toxicity. These data demonstrate that 8-Cl-cAMP synergistically increases the antiproliferative activity of taxanes and platinum-derived compounds and provide a rationale to use 8-Cl-cAMP in combination with taxanes and platinum-derived compounds.

Tags: Animal; Female; Human; Support, Non-U.S. Gov't

Major Descriptors: Antineoplastic Agents--Pharmacology--PD; *Apoptosis --Drug Effects--DE; *Cisplatin--Pharmacology--PD; * **Paclitaxel** --Pharmacology--PD; *Tumor Stem Cell Assay--Methods--MT; *8-Bromo Cyclic Adenosine Monophosphate--Analogs and Derivatives--AA

Minor Descriptors: Apoptosis--Genetics--GE; Cell Division--Drug Effects --DE; Drug Synergism; G2 Phase; Mice; Mice, Inbred BALB C; Mice, Nude; Mitosis; Neoplasm Transplantation; Transplantation, Heterologous; Tumor Cells, Cultured--Drug Effects--DE; 8-Bromo Cyclic Adenosine Monophosphate --Pharmacology--PD

CAS Registry No.: 0 (Antineoplastic Agents); 15663-27-1 (Cisplatin); 23583-48-4 (8-Bromo Cyclic Adenosine Monophosphate); 33069-62-4 (Paclitaxel); 41941-56-4 (8-chloro-cyclic adenosine monophosphate)

1/9/21
DIALOG(R)File 159:Cancerlit
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01317635 98642776
Clinical phase I study with Taxol (paclitaxel) **administered as 1-hour infusion (Meeting abstract).**
Mross K; Hauns B; Haring B; Bauknecht T; Meerpohl HG; Diergarten K; Maier-Lenz H; Unger C .
Tumor Biology Center, Freiburg i. Br., Germany
Proc Annu Meet Am Soc Clin Oncol; 16:A776 1997 ISSN 0732-183X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS; CLINICAL TRIAL; CLINICAL TRIAL, PHASE I
Journal Announcement: 199802
Subfile: ICDB/98642776
PAC is one of the major drugs for the **treatment** of breast, ovarian and lung cancer. Its anticancer efficacy is remarkable but its toxicity cannot be neglected as are there myelotoxicity, neurotoxicity, hypersensitivity reactions and asthenia. The toxicity seems to be schedule-dependent. 135 mg/m2 as 24-hour infusion or 175 mg/m2 as 3-hour infusion are the most often used application modes. We performed a phase I study m order to evaluate the toxicity and efficacy of a 1-hour infusion schedule. The pre-medication consisted of dexamethasone 20 mg iv, clemastine 2 mg iv and cimetidine 300 mg iv 1/2 hour before PAC was administered. Thirty-four patients with advanced pretreated **cancer** of different **types** (lung (n=16), breast (n=9), ovarian cancer (n=6) and three other) were included, starting with 150 mg/m2 (n=4), escalating to 175 mg/m2 (n=4), 200 mg/m2 (n=13), 250 mg/m2 (n=5) and de-escalating to 225 mg/m2 (n=8). The dose-limiting toxicity (DLT) was a grade 3 neurotoxicity at the maximum tolerated dose (MTD) level of 250 mg/m2 in two of three patients with somnolence and disorientation. Other toxicities (including all dose levels) were neutropenia, asthenia, myalgia, arthralgia grade 1-2, and hypersensitivity grade 1. Twenty-two patients were evaluable for anticancer efficacy evaluation (only patients receiving three complete cycles were considered). A partial response was seen m 5/22 (=23%), stable disease m 4/22 (=18%) and progressive disease in 13/22 (=59%). The PR were seen at dose levels of 175 up to 250 mg/m2. Due to the limited number of patients at each dose level, no final conclusion can be drawn as to the anticancer efficacy of the 1-hour infusion schedule of **taxol** . Since the DLT was seen at 250 mg/m2, we recommend 225 mg/m2 for phase II trials. Myelotoxicity was only modest, reinforcing the observation that the myelotoxicity of PAC is clearly schedule-dependent. It makes sense to compare the 3-hour and/or the 24-hour infusion with the 1-hour infusion with respect to the anticancer efficacy and toxicity of PAC. (C) American Society of Clinical Oncology 1997
CAS Registry No.: 0 (Antineoplastic Agents, Phytogenic); 33069-62-4 (Paclitaxel)

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01489296 99700810

A Phase I Study of Gemcitabine and Paclitaxel **in Patients with Solid Malignancies. (Meeting abstract).**

Glisson Shawn; Fleming Donal; Michelson G; Hendler FJ; Hadley T; Bhupalam L; Hargis Jeffrey; Rocca Renato V L
Department of Medicine University of Louisville, Louisville, KY.

Proc Annu Meet Am Soc Clin Oncol; 18:A814 1999
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
Journal Announcement: 199910
Subfile: ICDB/99700810

A phase I study was designed consisting of escalating doses of gemcitabine along with fixed-dose **paclitaxel** (150 mg/m2). The majority of patients enrolled were heavily pretreated with chemotherapy, radiotherapy or both. All patients were naive of the study drugs and possessed both adequate performance and end organ function. Eighteen patients were entered on the study. Characteristics included a median age of 66 (range 41 to 77) and advanced stage disease. The tumor **types** included colon **cancer** (6), bladder cancer (2), non-small cell lung cancer (3), esophageal cancer (2), pancreatic cancer (3), and cancer of unknown primary (2). **Paclitaxel** (150 mg/m2 over three hours) was given on day one and gemcitabine (800, 900, and 1000 mg/m2 over 30 min.) was given in three separate dose-escalating cohorts (1-3) on day one (following **paclitaxel** administration)and day eight. The **treatment** cycled every 21 days. The dose limiting toxicity (DLT) proved to be neutropenia, which limited the day eight administration of gemcitabine. [EMBEDDED TABLE] All non-hematologic toxicities were mild and included GI disturbances (nausea, vomiting, and diarrhea), dermatologic (rash) and neurologic (paresthesias) along with transient elevations of liver function tests. Four patients manifested an objective response (1CR, 3PR). In conclusion, the combination of gemcitabine and **paclitaxel** seems to be well tolerated and the recommended starting dose for a phase II study, in pretreated patients using a day one-day eight **treatment** schedule, should be 900 mg/m2 for gemcitabine (day one, day eight) along with 150 mg/m2 for **paclitaxel** (day one). (C) American Society of Clinical Oncology 1999.

1/9/8
DIALOG(R)File 159:Cancerlit
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01532264 99349536

The combination paclitaxel **, carboplatin and megestrol acetate is effective in women with recurrent uterine papillary serous adenocarcinoma.**

Eltabbakh GH; Moody J; Garafano LL; Hammond JM
Division of Gynecologic Oncology, University of Vermont, Burlington 05401, USA.

Eur J Gynaecol Oncol; 20(1):18-9 1999 ISSN 0392-2936 Journal Code: ENA
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 199909
Subfile: L; M MEDL/99349536

Uterine papillary serous adenocarcinoma is an uncommon and very aggressive **type** of endometrial **cancer** . A 76-year-old patient diagnosed with recurrent uterine papillary serous adenocarcinoma was prescribed megesterol acetate (160 mg daily), **paclitaxel** (135 mg/m2) and carboplatin (area under the concentration-time curve of 5) every 4 weeks for 4 courses. She demonstrated complete clinical response that was maintained for longer than 6 months with minimal toxicity. The combination megesterol acetate, **paclitaxel** and carboplatin may be effective in women with recurrent uterine papillary serous adenocarcinoma.

Tags: Female; Human
Major Descriptors: *Antineoplastic Agents, Combined--Therapeutic Use--TU; *Cystadenocarcinoma, Papillary--Drug Therapy--DT; *Endometrial Neoplasms --Drug Therapy--DT
Minor Descriptors: Aged; Carboplatin--Administration and Dosage--AD; Megestrol Acetate--Administration and Dosage--AD; **Paclitaxel** --Administration and Dosage--AD; Prognosis; **Treatment** Outcome
CAS Registry No.: 0 (Antineoplastic Agents, Combined); 33069-62-4 (Paclitaxel); 41575-94-4 (Carboplatin); 51154-23-5 (Megestrol Acetate)